CONTRIBUTORS

ANDERS, JAMES M., M.D.

BROWN, THOMAS R., M.D.

CLERF, LOUIS H., M.D.

DU BOIS, EUGENE F., M.D.

FRIEDENWALD, JULIUS, M.D.

FUTCHER, THOMAS B., M.D.

JACKSON, CHEVALIER, M.D., Sc.D.

LYON, B. B. VINCENT, A.B., M.D.

MARTIN, CHARLES F., M.D.

MOHLER, H. K., M.D.

OPIE, EUGENE L., M.D.

OSLER, SIR WILLIAM, Bart, M.D., F.R.S.

RIESMAN, DAVID, M.D.

ROLLESTON, SIR HUMPHRY DAVY, Bart., K.C.B., M.D. (Cantab.).

STENGEL, ALFRED, M.D.

STOCKTON, CHARLES G., M.D.

SUTHERLAND, COLIN G., M.D.

WOOD, EDWARD JENNER, B.Sc., M.D., D.T.M. (Eng.).

MODERN MEDICINE

ITS THEORY AND PRACTICE

IN ORIGINAL CONTRIBUTIONS BY AMERICAN AND FOREIGN AUTHORS

EDITED BY

SIR WILLIAM OSLER, BART., M.D., F.R.S.

LATE REGIUS PROFESSOR OF MEDICINE IN OXFORD UNIVERSITY, ENGLAND; HONORARY PROFESSOR OF MEDICINE IN THE JOHNS HOPKINS UNIVERSITY, BALTIMORE; FORMERLY PROFESSOR OF CLINICAL MEDICINE IN THE UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, AND OF THE INSTITUTES OF MEDICINE IN MC GILL UNIVERSITY, MONTREAL, CANADA

THIRD EDITION, THOROUGHLY REVISED

RE-EDITED BY

THOMAS McCRAE, M.D.

PROFESSOR OF MEDICINE IN THE JEFFERSON MEDICAL COLLEGE, PHILADELPHIA; FELLOW OF THE ROYAL COLLEGE OF PHYSICIANS, LONDON; FORMERLY ASSOCIATE PROFESSOR OF MEDICINE, THE JOHNS HOPKINS UNIVERSITY

ASSISTED BY

ELMER H. FUNK, M.D.

ASSISTANT PROFESSOR OF MEDICINE, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA

VOLUME III

DISEASES OF METABOLISM—DISEASES OF THE DIGESTIVE SYSTEM

ILLUSTRATED

LEA & FEBIGER

PHILADELPHIA AND NEW YORK

1926

COPYRIGHT
LEA & FEBIGER
1926

PRINTED IN U. S. A.

CONTRIBUTORS TO VOLUME III

JAMES M. ANDERS, M.D.,
Professor of the Theory and Practice of Medicine and of Clinical Medicine in the Medico-Chirurgical College, Graduate School of Medicine of the University of Pennsylvania; Consulting Physician to the Jewish Hospital Association of Philadelphia; Consulting Physician to the Widener Home for Crippled Children, Philadelphia; Officier de l'Instruction Publique; Chevalier of the Legion of Honor.

THOMAS R. BROWN, M.D.,
Associate Professor of Clinical Medicine in Johns Hopkins University; Physician-in-Charge of the Gastro-Intestinal Clinic and Associate Visiting Physician to Johns Hopkins Hospital, Baltimore, Md.

LOUIS H. CLERF, M.D.,
Instructor in Bronchoscopy and Esophagoscopy in Jefferson Medical College, Philadelphia; Assistant Professor in Bronchoscopy and Esophagoscopy in the Graduate School of Medicine of the University of Pennsylvania, Philadelphia; Assistant in the Bronchoscopic Clinic of Jefferson Hospital; Clinical Assistant in the Laryngological Dispensary of Jefferson Hospital; Assistant in the Bronchoscopic Clinic of the University Hospital; Adjunct Bronchoscopist at the Jewish Hospital, Philadelphia.

EUGENE F. DU BOIS, M.D.,
Medical Director of the Russell Sage Institute of Pathology, New York City; Associate Professor of Medicine in Cornell University Medical College, New York City; Director of the Second Medical Division of the Bellevue Hospital, New York City.

JULIUS FRIEDENWALD, M.D.,
Professor of Gastro-enterology in the University of Maryland, Baltimore, Md.

THOMAS B. FUTCHER, M.D.,
Associate Professor of Clinical Medicine in Johns Hopkins University; Assistant Visiting Physician to Johns Hopkins Hospital, Baltimore, Md.

CHEVALIER JACKSON, M.D., Sc.D.,
Professor of Bronchoscopy and Esophagoscopy in the Jefferson Medical College, Philadelphia; Professor of Bronchoscopy and Esophagoscopy in the Graduate School of Medicine of the University of Pennsylvania, Philadelphia; Bronchoscopist and Esophagoscopist in the Jefferson Medical College Hospital and the University of Pennsylvania Hospital; Lecturer on Bronchoscopy and Esophagoscopy in the Woman's Medical College of Pennsylvania, Philadelphia; Consultant Bronchoscopist and Esophagoscopist to the Samaritan Hospital, Temple University, the West Philadelphia Hospital for Women, the Germantown Hospital, the Philadelphia General Hospital, and the Philadelphia Municipal Hospital.

B. B. VINCENT LYON, A.B., M.D.,
Chief of Clinic in the Gastro-Intestinal Department of the Jefferson Hospital; Associate in Medicine in the Jefferson Medical College; Attending Physician (Formerly Pathologist) to the Methodist Episcopal Hospital, Philadelphia.

CHARLES F. MARTIN, M.D.,
Dean of the Faculty of Medicine and Professor of Medicine and Clinical Medicine in McGill University, Montreal, Canada; Physician to the Royal Victoria Hospital, Montreal, Canada.

H. K. MOHLER, M.D.,
Associate in Medicine in Jefferson Medical College; Medical Director of the Jefferson Hospital, Philadelphia.

EUGENE L. OPIE, M.D.,
Professor of Experimental Pathology in University of Pennsylvania; Director of the Laboratories at Henry Phipps Institute, Philadelphia.

SIR WILLIAM OSLER, BART., M.D., F.R.S.,
Late Regius Professor of Medicine in Oxford University, Oxford, England.

DAVID RIESMAN, M.D.,
Professor of Clinical Medicine in the University of Pennsylvania and the Philadelphia Polyclinic and College for Graduates in Medicine, Philadelphia.

SIR HUMPHRY DAVY ROLLESTON, BART., K.C.B., M.D. (CANTAB.),
Regius Professor of Physic in Cambridge University, Cambridge, England; President of the Royal College of Physicians of London; Physician in Ordinary to H. M. the King; Emeritus Physician to St. George's Hospital, London, England.

ALFRED STENGEL, M.D.,
Professor of Medicine in University of Pennsylvania, Philadelphia.

CHARLES G. STOCKTON, M.D.,
Emeritus Professor of Medicine in the Medical Department of the University of Buffalo, Buffalo, New York; Consulting Physician to the Buffalo General Hospital and the New York State Hospital for Crippled and Deformed Children.

COLIN G. SUTHERLAND, B.A., M.D.,
Clinical Assistant at the Royal Victoria Hospital, Montreal, Canada; Demonstrator of Medicine at McGill University, Montreal, Canada.

EDWARD JENNER WOOD, B.Sc., M.D., D.T.M. (ENG.),
Consulting Physician to the James Walker Memorial Hospital, Wilmington, North Carolina and the State Hospital, Raleigh, N. C.; Member of the Association of American Physicians; Fellow of the Royal Society of Tropical Medicine, etc.

CONTENTS

PART I

DISEASES OF METABOLISM

CHAPTER I

METABOLISM FROM THE POINT OF VIEW OF THE PRACTITIONER 17
By Eugene F. Du Bois, M.D.

CHAPTER II

DIABETES MELLITUS AND INSIPIDUS 116
By Thomas B. Futcher, M.D.

CHAPTER III

GOUT 178
By Thomas B. Futcher, M.D.

CHAPTER IV

OBESITY 209
By James M. Anders, M.D.

PART II

DISEASES OF THE DIGESTIVE SYSTEM

CHAPTER V

INTRODUCTORY DISCUSSION ON THE DISEASES OF THE DIGESTIVE APPARATUS 223
By Charles G. Stockton, M.D.

CHAPTER VI

DISEASES OF THE MOUTH AND SALIVARY GLANDS 245
By David Riesman, M.D.
Revised by Henry K. Mohler, M.D.

CHAPTER VII

DISEASES OF THE ŒSOPHAGUS 283
By Chevalier Jackson, M.D., D.Sc., and Louis H. Clerf, M.D.

CHAPTER VIII

FUNCTIONAL DISEASES OF THE STOMACH 307
By Julius Friedenwald, M.D.

CHAPTER IX

ORGANIC DISEASES OF THE STOMACH 371
By Charles F. Martin, M.D. and Colin Sutherland, M.D.

CHAPTER X

DISEASES OF THE INTESTINES 495
By Alfred Stengel, M.D.

CHAPTER XI

SPRUE 649
By Edward Jenner Wood, M.D.

CHAPTER XII

DISEASES OF THE PANCREAS 657
By Eugene L. Opie, M.D.

CHAPTER XIII

DISEASES OF THE LIVER, GALL-BLADDER, AND BILIARY DUCTS 715
By the Late A. O. J. Kelly, M.D.
Revised by B. B. Vincent Lyon, M.D.

CHAPTER XIV

DISEASES OF THE PERITONEUM 894
By Sir Humphry Rolleston, Bart., K.C.B., M.D., F.R.C.P.

CHAPTER XV

SPLANCHNOPTOSIS, VISCEROPTOSIS, ENTEROPTOSIS, GLÉNARD'S DISEASE 986
By Thomas R. Brown, M.D.

PART I

DISEASES OF METABOLISM

CHAPTER I

METABOLISM FROM THE POINT OF VIEW OF THE PRACTITIONER

By EUGENE F. DU BOIS, M.D.

It is obviously impossible to cover the whole field of nutrition in an article which forms only a small part of a system of medicine. We may eliminate almost entirely certain branches of this broad science, such as food economics, and because most practitioners are not familiar with the details of modern chemistry, it seems advisable to omit the chemical discussions that occupy a large amount of space in most of the text-books. The clinician's time may be limited, but it is quite essential that he should keep abreast of the recent advances in the knowledge of metabolism. Bearing this in mind, we shall try to review the fundamental principles in such a manner that they may be applied to clinical problems and also to the interpretation of the experimental work. The reader can rest assured that it saves time to master the general principles rather than the various dietary fads and fancies which may attract undue attention. For instance, during the last few years there has been a rather general impression that the discovery of the vitamines has revolutionized the whole science of nutrition. It is true that this discovery is a matter of great importance, but it has merely added another chapter to the subject without detracting in the slightest from the importance of the older conceptions.

History of Metabolism.—It is difficult, if not impossible, to base the practical applications of nutrition on a purely scientific foundation. The dietary habits of the community are firmly established by the customs which have descended from previous generations. Even those who have studied metabolism for many years retain the prejudices of their parents and remember, perhaps subconsciously, the admonitions they received in childhood. Our daily food, like our clothing, is therefore the heritage of past ages. Our remote ancestors in different parts of the world lived on such food as they could obtain by hunting and fishing, supplemented by fruits, tubers, and by the cultivation of meagre crops. With the development of agriculture and herds of dairy cattle, men obtained a larger proportion of their energy supply from carbohydrate

and butter fat. The modern improvements in transportation and canning added a greater supply of fruits and green vegetables. There are still, however, many parts of the world in which the natives subsist as did our prehistoric ancestors. Their good health and capacity for great exertion demonstrate clearly that man can utilize a wide range of foodstuffs. It shows that there is a large factor of safety and that we must not be too positive in our statements that one particular form of dietary is better than another. The Eskimo lives almost exclusively on meat, with large amounts of fat; the Bengali on rice, with a small amount of fish. It is quite probable that these rations could be followed by many individuals in our large cities without noticeable impairment of health.

The history of metabolism has recently been reviewed in a delightful fashion by Lusk,[1] and the reader who is particularly interested is referred to his article. Before Lavoisier (1743–1794) the knowledge of metabolism was chaotic and the student who was familiar with the literature of that time knew little more than the housewife; perhaps he knew less because his mind was filled with false ideas. Lavoisier first demonstrated the significance of oxygen, carbon dioxide, and their relationships to the combustion of food and the production of heat. By careful experiments, with a technique that would be considered excellent even today, he demonstrated the main facts regarding the basal metabolism and the increase in heat production caused by exposure to cold, by the ingestion of food, and by muscular exercise. After Lavoisier the work was carried on by many investigators, who gradually developed our knowledge of the subject. Clinicians are particularly indebted to Regnault and Reiset who in 1849 published their work on the metabolism of animals, with a description of a closed-circuit apparatus which measured the consumption of oxygen and the production of carbon dioxide. The general principles of this device are still embodied in most of the machines now used in the clinic for determining the basal metabolism. Regnault and Reiset grasped the significance of the respiratory quotient, the volume of carbon dioxide excreted divided by the volume of oxygen absorbed, and demonstrated its relationship to the kind of food that was being metabolized. In the middle of the last century the field was dominated by Liebig, who divided the foodstuffs into proteins, fats, and carbohydrates and stated that it was protein which furnished the energy for muscular work. This erroneous conception persists even to the present day in the minds of a large proportion of the laity, who firmly believe that men doing hard work should consume a large amount of meat. Liebig made great contributions to our knowledge of the combustion of various foodstuffs and showed how each furnished its quota of calories. Bidder and Schmidt, in 1852, discovered many new facts regarding the digestive juices and metabolism. They recognized that each animal has a typical minimum of necessary metabolism which was apparent in experiments when no food was given, and they developed the modern method of determining the total metabolism from the analysis of urine, feces, and the gases of respiration.

[1] Barker's *Endocrinology and Metabolism*, Appleton & Co., New York, 1922, **3**, 3–78.

Carl von Voit (1831–1909), of Munich, may be considered the founder of the modern science of metabolism. He worked in the same university as von Pettenkofer, who constructed a large respiration chamber in which a man could live and work for several days. Together they made a long series of careful experiments to determine the income and output of energy of animals and men. Voit proved that muscular work did not increase the protein metabolism and showed that its chief function was to replace the tissues of the body, which were continually being broken down at a slow but steady rate. He showed that the unknown causes of metabolism are found in the cells of the organism. The energy for the cells may be furnished by protein alone or by little protein and much carbohydrate and fat. It is impossible to enumerate here all the contributions of Voit, but it is sufficient to say that he was able to demonstrate most of the important facts in metabolism known at the present time. With Pettenkofer he studied a few patients with various diseases but his apparatus was not well adapted to this work.

Voit's pupil, Max Rubner (1854—) advanced the science materially. He for the first time built a respiration chamber which was also a calorimeter and was thus able to calculate the heat production not only from the gases of respiration (indirect calorimetry), but also by the direct measurement of the heat of radiation, conduction and vaporization (direct calorimetry). He proved that carbohydrate and fat, oxidized in the body, gave off exactly the same amount of heat as when oxidized in a bomb calorimeter. Protein was not completely oxidized, since some potential energy was lost in the urea. By this calorimeter Rubner established the fact that the law of the conservation of energy applied to animals. Rubner made extensive studies on various dietaries and determined their heat values and the percentages absorbed by the gastro-intestinal tract. Taking into consideration the proportions in which the various foods enter into our diet, he suggested the following average calorific values: 1 gram of protein furnishes 4.1 calories; 1 gram of carbohydrate furnishes 4.1 calories; 1 gram of fat furnishes 9.3 calories. These figures allow for only a small portion of the loss in the feces. Although there are certain inaccuracies in the standard figures with some foods, they have been found on the whole to be exceedingly satisfactory and are still used in most of our calculations. Rubner was the first to make extensive studies of the rise in metabolism which follows the ingestion of food. This he called the "specific dynamic action," a term which has persisted although it is perhaps somewhat inappropriate. Rubner also developed contemporaneously with Richet, the law of surface area which had been foreshadowed in the writings of several earlier investigators. This law states that the metabolism of resting animals is proportional to their surface area. Inanimate objects which are warmer than the surrounding air lose heat at a rate which is proportional to their surface. In animals, the relationship between the surface and heat loss is more complicated because of the nature of the integument and the regulation of the blood flow. Rubner showed that the heat loss of animals does not change appreciably during the ordinary ranges of air temperature.

Clinicians are particularly indebted to Nathan Zuntz (1847–1920), who,

with Geppert devised an apparatus which determined, by air analysis, the consumption and carbon dioxide production of individuals during periods of ten to twenty minutes or longer. Using short experiments, he was able to study men at complete muscular repose. With Loewy he laid the foundations for the modern experimental procedure in determining the basal metabolism. Magnus-Levy, a pupil of Zuntz, carried this technique into the clinic and, in a few years, not only established a fairly satisfactory series of normal controls, but also discovered most of the important facts regarding the respiratory metabolism in disease.

In America, the first important work in metabolism began when Atwater undertook the construction of a respiration calorimeter for man. He was fortunate in securing the coöperation of Rosa, the physicist, who added much that was new to the methods previously employed, and of Francis G. Benedict, who not only improved the original calorimeter, but continually developed new and better types of apparatus. Atwater and Benedict, with their associates, were able to keep men in the calorimeter for many days at a time, measuring the food consumption during rest and during periods of work on a stationary bicycle. Later this investigation was transferred to the Nutrition Laboratory in Boston, a branch of the Carnegie Institution of Washington. There, under the leadership of F. G. Benedict a large staff of workers have made numerous studies on diabetics, on fasting men and particularly on normal controls.

Lusk, a pupil of Voit, has established a centre for the study of respiratory metabolism at Cornell University Medical College in New York City. With an unusually accurate respiration calorimeter he has studied the phenomena of the specific dynamic action of foods. He has also established the calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital where particular attention has been given to the phenomena of disease. In recent years important contributions to the study of the metabolism of children have been made by Hasselbalch, Murlin, Benedict and Talbot. Many important clinical studies have been made by Grafe and Rolly, Means and Aub, Joslin, and Boothby and Sandiford and others.

This brief review has scarcely touched on the extensive work on the physiology of digestion or the brilliant studies on physiological chemistry by such men as Salkowski, Emil Fisher, Abderhalden, Chittenden, Mendel, Folin, S. R. Benedict, and many others. We must not forget our indebtedness to the roentgenologists who have taught us much regarding the intestinal tract, nor to the group of men who have studied the vitamines.

Methods of Investigation.—Many crude observations on the quantities and varieties of food necessary to maintain life must have been made soon after the dawn of civilization. We can conceive the economical slave drivers of Egypt trying to determine the cheapest food that would keep the men working efficiently. This method is still used in many institutions at the present time. Field studies of similar nature, when carefully made, are perhaps better than pseudoscientific studies with faulty technique due to uncontrollable factors.

There have been many field studies in nutrition which have given us a great deal of information about the dietary habits of various commu-

nities. The observer determines the food consumption of an individual or a family or a group of men by measuring the food purchased and the waste. He estimates the calories and the nitrogen content of the food and he may determine the nitrogen output by analyzing the urine. If the individuals remain in approximate weight- and nitrogen-balance over a period of several weeks, it is assumed, not always too correctly, that the intake has been just sufficient to cover the expenditure. The possible sources of error in this type of experiment are obvious. It is difficult to weigh accurately each foodstuff and to estimate its composition, since this varies greatly in many cases. We can never be certain that individuals who are not locked up do not take some extra food. The collection of urine may not be complete. Moreover, the maintenance of a constant body weight is sometimes found where considerable amounts of fat have been replaced by water. Weight-balance experiments are notoriously inexact unless long periods are used. Notwithstanding these objections, we have learned much from such field experiments but they are significant only if performed on a large number of individuals.

The clinician may in this same manner determine the food intake of a patient and perhaps make a rough estimate of the output of energy if the patient remains in weight- and nitrogen-balance. Unless the experiment is a long one, it is doubtful if the evaluation of the total energy requirement is any more accurate than an estimation of the calories of the basal metabolism plus a guess as to the extra calories due to the food and the muscular activity. In a general ward a balance of the intake and output of carbohydrate or nitrogen is no more accurate than the least reliable part of the experiment. This weakest link is usually the intelligence of the patient and the nurse, orderly, or ward maid.

Experiments which depend entirely on the measurement of food and analysis of urine are of little service in finding the total caloric output, but they may give much information regarding the protein and mineral metabolism. They are best conducted in a metabolism ward with a special staff of nurses. Such a ward is maintained by the Russell Sage Institute of Pathology in Bellevue Hospital, and the technique is still the same as that described by Gephart and Du Bois[1] ten years ago.

In this particular ward there are four beds and a balcony where patients can sit outdoors. Several highly trained nurses take turns watching the patients night and day, never letting them leave the ward. All the food is prepared by these same nurses, who weigh the foods raw, cook them in enamelware dishes, and serve them to the patients in these same dishes. The nurses study the likes and dislikes of each patient and give him only such food as he can consume. There is no residue left on the plates. They use only simple hospital foods which have been shown by frequent analyses to vary but little in composition. Skill in cooking gives sufficient flavor and variety.

The urine is collected with great care. The patients, who are all males, void directly into 20-ounce, wide-mouthed bottles. Each voiding is kept separate and preserved with thymol or toluene. In the morning, at the

[1] *Arch. Int. Med.*, 1915, **15**, 829.

end of the twenty-four-hour period, the voidings for the day are united and a determination made of the total nitrogen, etc.

Feces, in some experiments, are passed directly into weighed buckets, and then treated with a little formalin before drying. On starting an experimental period 5 grains (0.3 gm.) of powdered carmine is given with the first meal of the new diet and the feces are saved as soon as the carmine makes its appearance. In all work on the absorption of food it is necessary to use periods at least three or four days long, preferably longer. Patients are weighed daily at the same time of day on a "silk scale" which is accurate to 10 gm. Bed patients are transferred to a platform which is placed on the scales.

Since this ward is used chiefly in association with the Sage respiration calorimeter which is in the next room, the basal metabolism of many of the patients is known. In the other cases the basal metabolism is estimated from the height, weight, and age. To the basal calories is added an amount which is estimated will cover the carefully controlled activities of the patient. Even under the ideal conditions of this ward there is a large error in the estimation of the calories expended in each twenty-four-hour period. Exact determinations can be made only if the patient lives in a respiration chamber.

The protein actually metabolized by the subject is determined by multiplying the grams of urinary nitrogen by 6.25. The resulting figure may be quite different from the protein intake, since the individual may be storing protein or losing it from his own tissues. The number of grams of carbohydrate and fat actually metabolized can be determined only by respiration experiments, and here also the figures may differ greatly from those of the intake.

This brings us to a consideration of the principles of respiration apparatus.[1] We can calculate the metabolism from the gaseous exchange within the body. Starch is a polysaccharide with a formula which may be expressed simply as $(C_6H_{10}O_5)_x$. When oxidized either within or without the body 1 molecule of starch unites with 6 of oxygen, as follows:

$$C_6H_{10}O_5 + 6O_2 = 6CO_2 + 5H_2O.$$

Substituting the molecular weights of these substances, we find

$$162 \text{ starch} + 192 \text{ oxygen} = 264CO_2 + 90H_2O.$$

Since 1 gm. of starch furnishes 4.2 calories, 162 gm. will produce 680.4 calories. Since each gram of oxygen represents 0.6997 litres we find that, in the production of 680.4 calories from starch, 134.34 litres of oxygen have been consumed. This means that each litre of oxygen so utilized represents 5.065 calories.

The molecules of CO_2 produced in the reaction are exactly equal to the

[1] For greater detail the reader is referred to G. Lusk: *The Elements of the Science of Nutrition*, 3d ed., Saunders & Co., Philadelphia, 1917; E. F. Du Bois: *Basal Metabolism in Health and Disease*, Lea & Febiger, Philadelphia, 1924; F. G. Benedict: *Methoden zur Bestimmung des Gaswechsels bei Tieren und Menschen, Abderhalden's Handbuch der biologischen Arbeitsmethoden*, IV, Part 10, Urban & Schwarzenberg, Vienna, 1924.

molecules of oxygen consumed. This means that the respiratory quotient for starch

$$(\text{R. Q.} = \frac{\text{Vol. } CO_2}{\text{Vol. } O_2}) \text{ is 1.00.}$$

The reaction for a typical fat, such as tripalmitin, is as follows:

$$\underset{806}{C_{51}H_{98}O_6} + \underset{2320}{72.5O_2} = \underset{2244}{51CO_2} + \underset{822}{49H_2O} \quad \text{molecular weights.}$$

In the case of protein, the calculation is more complicated, since we must allow for the elimination of urea in the urine. Calculating the reactions for the various foodstuffs we obtain, in the manner outlined above, the following table, which forms the basis of all respiration experiments:

TABLE I.

	Calories per gram oxidized.	R. Q.	Caloric valué of 1 litre. Oxygen.	Caloric valué of 1 litre. CO_2.
Carbohydrate	4.1	1.00	5.047	5.047
Fat	9.3	0.707	4.686	6.629
Protein	4.1	0.801	4.485	5.579

One gram of urinary nitrogen represents the oxidation of 6.25 grams of protein, or 26.51 calories from protein.

The figures given above are the standards used in most laboratories. They differ slightly from the calculations made according to the written formulæ due to the fact that different authorities select fats, proteins, etc., of different chemical composition and also use slightly different constants for physical measurements. Since divergencies as great as 1 per cent. are often found in the basic calculations, it is clear that an error of 1 per cent. may exist in any respiration experiment.

In the table given above we note than the calorific value of a litre of oxygen is almost the same for the three foodstuffs. This means that, for each litre of oxygen consumed by the individual during a given period, there has been liberated an amount of heat somewhere between 4.48 and 5.05 calories. If the subject is studied under basal conditions, twelve or more hours after food, we may take an average figure of 4.825 and obtain a result which is within 1 or 2 per cent. of the correct figure. This is the procedure used with the Benedict portable apparatus and others of its type and is accurate enough for clinical purposes.

More exact calculations can be made if we determine also the carbon dioxide excretion, thus obtaining the respiratory quotient for the total mixture of protein, fat, and carbohydrate being utilized. It is then necessary to find the grams of each of these substances consumed during the period. In the case of protein this is simple if we collect the urine for a period of two hours or more and find the total nitrogen content. The grams of urinary nitrogen multiplied by 6.25 represent with fair accuracy the protein metabolized during this period. It is then easy to calculate the oxygen and carbon dioxide involved in the metabolism of this protein. This leaves the non-protein carbon dioxide and oxygen, which give us

the respiratory quotient due to the metabolism of fat and carbohydrate. By a table of calculations, which will be found in the standard text-books on metabolism, we can determine, from the quotient, the exact proportion and the actual number of grams of fat and carbohydrate metabolized. This is the method of indirect calorimetry used with the respiration calorimeter or the Tissot apparatus. In some clinics the urinary nitrogen is not determined and it is assumed that protein furnishes 15 per cent. of the calories. For experimental work it is obviously of great advantage to know exactly how many grams of protein, fat, and carbohydrate are metabolized in each period and the percentage of total calories furnished by each foodstuff.

RESPIRATION APPARATUS

Strictly speaking, the only type of apparatus which should be called a calorimeter is one which measures heat by the direct or physical method. In recent years, however, in this country, the term is being applied to the smaller machines which employ the method of indirect calorimetry.

The Pettenkofer-Voit Respiration Chamber.—This consisted of a small room in which a man could live for several days. Air was drawn through the apparatus at a measured rate and samples of the ingoing and outgoing air analyzed to determine the water vapor and carbon dioxide. The oxygen consumption was measured indirectly and rather inaccurately.

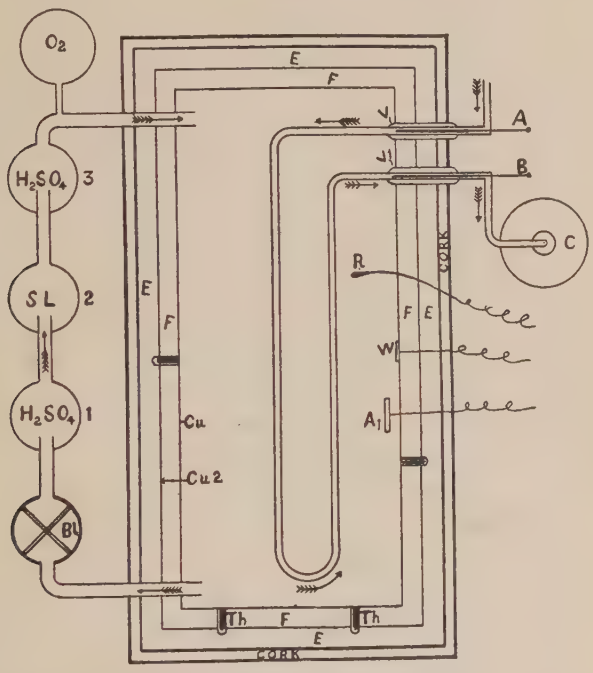
Atwater-Rosa-Benedict Respiration Calorimeter. — The most recent example of this apparatus is the calorimeter of the Russell Sage Institute of Pathology in Bellevue Hospital[1] in a room next to the metabolism ward. The box is about the size of a lower berth of a Pullman sleeping car. In this the patients are sealed for periods of two to six hours. The diagram shows the method of ventilation. Air is withdrawn from the foot of the chamber by a blower. It is driven through a bottle of sulphuric acid, which removes all the water vapor, next through a bottle of soda-lime, which removes the carbon dioxide, and then through sulphuric acid, which catches the moisture given off by the soda-lime. These bottles are weighed each hour to determine the grams of water and carbon dioxide eliminated. The air thus purified is returned to the head of the box and used over and over again. As the subject consumes oxygen this gas is added automatically from a bomb which is weighed each hour. Corrections must be made for changes in temperature and barometric pressure.

The measurement of heat by the direct or physical method is as follows: A constant stream of cold water is conducted through pipes which run just below the ceiling of the calorimeter. This water removes all the heat given off by radiation and conduction. The temperature of the water is measured as it enters the calorimeter and as it leaves, and we can obtain the calories directly by multiplying the liters of water flowing each hour by the number of degrees Centigrade which the water has been heated. To this we must add the calories lost through the vaporization of water. Each gram of water vaporized at the calorimeter temperature (20° to

[1] Lusk, G.: *Arch. Int. Med.*, 1915, **15**, 793; Riche, J. A., and Soderstrom, G. F.: *Ibid.*, p. 805.

23° C.) represents the loss of about 0.586 calories. We therefore use this factor to multiply the grams of water removed by the first sulphuric acid bottle. An additional correction must be made for heat stored in or lost from the body of the subject if his temperature has changed during the experimental period.

FIG. 1



Schematic diagram of the Atwater-Rosa-Benedict respiration calorimeter.

Ventilating system: Bl., blower to keep air in circulation; 1, H_2SO_4 to remove moisture given off by patient; 2, soda-lime to remove CO_2; 3, H_2SO_4 to catch moisture given off by soda-lime; O_2, oxygen introduced as consumed by subject.

Indirect calorimetry: Increase in weight of H_2SO_4 (1) = water elimination of subject; increase in weight of soda-lime (2) + increase on weight of H_2SO_4, (3) = CO_2 elimination; decrease in weight of oxygen tank = oxygen consumption of subject.

Heat-absorbing system: A, thermometer to record temperature of ingoing water; B. thermometer to record temperature of outgoing water; V, vacuum jacket; C, tank for weighing water which has passed through calorimeter each hour; W, thermometer for measuring temperature of wall; A_1, thermometer for measuring temperature of the air; R, rectal thermometer for measuring temperature of subject.

Direct calorimetry: Average difference of A and B × liters of water + (gm. water eliminated × 0.586) + (change in temperature of wall × hydrothermal equivalent of box) + (change of temperature of body × hydrothermal equivalent of body) = total calories produced.

Th, thermocouple; *Cu*, inner copper wall; Cu_2 outer copper wall; *E*, *F*, dead air spaces.

The accuracy of the calorimeter is tested at regular intervals by burning a known amount of alcohol and calculating the theoretical production of heat, carbon dioxide, and water, and the consumption of oxygen. The amounts of heat, carbon dioxide, and oxygen actually measured almost invariably check within 1 per cent. of the theoretical in the three-hour period. The errors during individual hours are sometimes as great as

4 or 5 per cent., though usually less than 2 per cent. There is a larger error in the determination of water, since this is absorbed by the objects within the calorimeter. In human experiments the methods of direct and indirect calorimetry agree within 1 per cent. if the totals are taken for a large series of experiments. In individual hours, or even in three-hour periods, there may be a divergence of 5 per cent. or even more, since it is difficult to measure exactly the amount of heat stored in or lost from the body. In short observations indirect calorimetry is more exact than direct, and the close agreement of the total figures obtained in a large series of experiments with various diseases proves the chemical method of estimating heat production essentially sound, since it corresponds with the standard method which employs physical measurements.

Respiration calorimeters are now used only for experimental work, since they are expensive in construction and operation. They alone can tell us the facts regarding the mechanism of the rise and fall of body temperature. They are probably the most accurate of all types of respiration apparatus, and we must remember that their errors of 1 or 2 per cent. are often exceeded in determinations made with other types of machines.

Benedict Cot-chamber.—This resembles in general construction the Atwater-Rosa-Benedict calorimeter without the elaborate devices necessary for the measurement of heat by the direct method. The patient lies in a metal box for a period of one or more hours.

Closed-circuit Apparatus.—Benedict Universal (Unit Apparatus).—It is not necessary to have the patient in a closed chamber if an air-tight joint can be made between his lungs and the system of bottles which measure the production of carbon dioxide and absorption of oxygen. Such a joint can be made by a tight mask, by nose-pieces, or better, by a mouth-piece. The gas-absorption system is a small replica of that used with the calorimeter. The experimental period is ten to twenty minutes. This rather elaborate machine has been almost entirely supplanted by simpler ones which do not measure the carbon dioxide.

Benedict Portable Apparatus.—Benedict has emphasized the fact that for clinical purposes the results are sufficiently accurate if we determine the oxygen alone and assume for basal experiments that the respiratory quotient will be about 0.82 and the calorific value of a litre of oxygen, 4.825. He therefore devised a simple and inexpensive machine with bottles which remove but do not measure the carbon dioxide. There is a small spirometer which is filled with a mixture of air and oxygen at the beginning of the experiment. The patient is attached to this by means of a mouth-piece and, as he absorbs oxygen, the level of the spirometer falls a little at the end of each expiration. The extent of this fall can be measured over a period of six to ten minutes, giving us with considerable accuracy the oxygen consumption.

Benedict's original Portable has been modified somewhat by Sanborn, by Collins, and more recently by Roth who has substituted gas-mask valves for the small electric blower which kept the air in circulation. The blower is expensive and rather troublesome at times. The gas-mask valves cause a slight resistance to breathing, but apparently not enough to affect the results.

Student Apparatus.—F. G. and C. G. Benedict have recently simplified the Portable still further and made a very inexpensive model which they do not yet recommend for clinical work, though it may prove to be sufficiently accurate.

Jones Metabolimeter.—This is an extremely ingenious small machine which delivers a known amount of oxygen into a bag and determines the length of time required for its absorption by the body.

McKesson Metabolor.—This resembles in principle the Benedict Portable, but employs the Krogh type of wedge-shaped spirometer.

Krogh Apparatus.—August Krogh, of Copenhagen, who is one of the leaders in metabolism investigation, devised independently a machine quite similar to the Benedict Portable without an electric blower. He employed his wedge-shaped spirometer and rubber valves.

With the Benedict and Krogh types of apparatus much more accurate results can be obtained if graphic records are made of the respiration. The kymographic attachments are expensive but quite essential. Benedict emphasized their importance many years ago.

Open Circuit Apparatus.—Zuntz-Geppert Apparatus.—This was employed by Magnus-Levy when he laid the foundations of our knowledge of the respiratory metabolism in disease. The expired air passes through a gas meter and a continuous sample is automatically collected. This is then analyzed for carbon dioxide and oxygen. The machine is complicated and the technique difficult; the results are therefore not reliable except in the hands of master workmen like Magnus-Levy.

Tissot Spirometer.—Tissot collects the expired air in a large metal spirometer which, by means of an ingenious counterpoise, is balanced in all positions. The subject breathes through a mask or mouth-piece. Valves are attached so that he inspires outdoor air led into the room through a large pipe. The expired air is measured in the spirometer and a sample removed for analysis of the oxygen and carbon dioxide. In this country improvements have been added by C. V. Bailey and Boothby and Sandiford. It is probably the best device for measuring the metabolism in short periods since it gives both carbon dioxide and oxygen. The disadvantages are the expense of the spirometer and the difficulty in training technicians in the art of air analysis.

Douglas Bag.—Instead of using a metal spirometer Douglas employs a large rubber bag to collect the expired air. This is later measured in a gas meter. The apparatus has the advantage of being light and fairly inexpensive. It is much used in England.

King Apparatus.—From the time of Voit until about 1912 metabolism results were usually expressed in terms of carbon dioxide elimination per minute. Later investigators abandoned this as a standard because the calorific value of a liter of carbon dioxide varies considerably with the character of foodstuff metabolized. It was noted also that any increase in the ventilation of the lungs tended to wash out of the blood and tissues considerable amounts of carbon dioxide which are there loosely held in storage. J. T. King, of Baltimore, revived the carbon dioxide method. By an open-circuit apparatus of simple construction he collects and weighs this gas and in basal experiments employs a calorific value which assumes

a respiratory quotient of about 0.82. It seems doubtful if this method can be as satisfactory as those which determine the oxygen.

MANAGEMENT OF BASAL METABOLISM TESTS

The *basal metabolism* may be defined as the level of heat production determined with the subject lying absolutely motionless in the morning fourteen hours or more after the last meal. Krogh suggested that the term "standard metabolism" would be better, since the so-called basal metabolism does not really represent a minimum. Lower figures would be obtained during profound sleep in the early morning hours; still lower figures, if we could stop the activity of the heart, lungs, kidneys, etc., and measure only the resting metabolism of the cells. Since it is impractical to measure the metabolism during profound sleep, we use as a standard the metabolism between the hours of 8 A.M. and noon. Complete muscular relaxation is absolutely essential and we must also exclude the effect of previous activity by having the patient rest after he reaches the laboratory until the pulse-rate reaches its normal constant level. We must also exclude the stimulating effect of mental excitement and take every precaution to reassure the patient and allay apprehension or nervousness. This is best done by a dummy experiment the day before the real test. The stimulating effect of food usually ceases twelve hours after the last meal, but may be evident for a few hours longer if a large amount of protein was consumed the previous evening. It has been shown that a small breakfast consisting of 30 gm. of bread, 8 gm. of butter, a cup of caffeine-free coffee with 10 gm. of sugar, and 60 cc. of milk may be given three hours before the test without significant change in the metabolism. Dr. and Mrs. Benedict[1] suggested an improved breakfast consisting of 1 cup (200 cc.) of caffeine-free coffee, 16 mg. of saccharin, 30 gm. of medium cream and 25 gm. of potato chips. It is seldom advisable to allow the patient anything except a cup of caffeine-free coffee without milk or sugar on the morning of the test, since he may take too much food if given any leeway.

Great care must be given to the technique and all apparatus must be tested frequently for leaks. The determinations of oxygen consumption should be made in triplicate, and results mistrusted unless they agree within 5 per cent. In all important or doubtful cases the tests should be repeated on another day. Every technician must collect a large series of his own normal controls and compare them with the standards in other laboratories. The practitioner who uses the results of the metabolism test should scrutinize these normal controls in order to familiarize himself with the rather wide variation in normal individuals.

Experiments on Muscular Work.—It is obvious that the basal metabolism forms only a fraction, sometimes a small one, of the total metabolism. Experiments to determine the influence of other factors may be performed in respiration chambers or the subjects may be attached to one of the smaller machines by masks or mouth-pieces. The work performed

[1] *Boston Med. and Surg. Jour.*, 1923, **188**, 849.

in some cases is measured quantitatively by having weights lifted a known distance a certain number of times a minute or by having the subject walk on a treadmill. Many of the best experiments have been made using a bicycle ergometer which permits an exact determination of the work accomplished. If the heat production of the subject is determined by indirect calorimetry at the same time, it is possible to determine the calories in excess of the basal level required for the performance of a certain task.

Experiments on the Effect of Foods.—The basal metabolism of the animal or human subject is first determined either on the morning of the food experiment or else calculated from the average of several closely agreeing results obtained on other days. The food in question is then administered and the curves of the nitrogen elimination and heat production followed for several hours. It is necessary to calculate the grams of protein, fat, and carbohydrate metabolized each hour and to take into consideration not only the quantities of the foodstuffs administered but also the quantities actually oxidized. Some of the food given may be stored without affecting the metabolism.

Experiments on the Vitamines.[1]—In testing the vitamine content of various foods laboratory animals are employed. In the case of the antineuritic vitamine (water-soluble B) we may first produce polyneuritis in a pigeon by a diet of polished rice. When the disease has developed we can then determine the amounts of various substances which will effect a cure. We may also determine just how much of a certain foodstuff must be added to a diet of polished rice to prevent the development of neuritis. In this country the young white rat is usually employed in tests for fat-soluble A and water-soluble B. This animal has been so carefully studied that we know the normal rate of growth and the minimal amounts of various foods necessary for this growth. There are several basal diets which are palatable, digestible, and contain enough protein, fat, carbohydrate, and mineral salts to supply the needs of the growing animal. The protein, usually casein, is carefully purified, likewise the starch and lard. In such a diet there is a complete absence of vitamines A and B and these must be added in order to secure proper growth and absence of symptoms of avitaminosis. We can add an excess of one of these vitamines and determine how much of a given food must be administered to supply a sufficient amount of the other vitamine. Rats are not subject to scurvy and therefore cannot be employed for experiments on "water-soluble C," the antiscorbutic factor. Guinea-pigs are used for these tests.

Experiments on Amino-acids and Incomplete Proteins.—Animals will not grow normally unless the food contains certain amino-acids, such as tryptophane and lysine. These are lacking in some of the incomplete proteins, such as zein of maize. In the basal diet for young white rats outlined above casein, a complete protein, was used. For this we may substitute the protein or mixture of amino-acids to be tested, making

[1] For details consult Eddy, W. H.: *The Vitamine Manual*, Williams & Wilkins, Baltimore, 1922; Mendel, L. B.: *Nutrition. The Chemistry of Life*, Yale University Press, New Haven, 1923; Funk, C.: *The Vitamines*, Williams & Wilkins, Baltimore, 1922.

sure that the animals are receiving sufficient calories and a plentiful supply of vitamines A, B, and C. Failure of growth indicates that there is a lack of some essential amino-acid. Additional proof is secured by adding to the diet the pure substance in question or else some form of protein which contains it. Growth should then be resumed at a normal or accelerated rate.

Observations on Infants.[1]—In the study of the respiratory metabolism of children the difficulties are numerous. Infants will not remain quiet unless they have a stomach full of food. This makes it almost impossible to secure true basal conditions twelve or more hours after the test meal. Infants are practically never quiet unless asleep and sleep introduces another unknown factor. It is impossible to use mouth-pieces or masks with children and we must resort to small calorimeters or respiration chambers. Howland used Lusk's dog calorimeter and found that the methods of direct and indirect calorimetry agreed closely. Murlin built a respiration chamber inside a Frease incubator. Benedict and Talbot used a small cot chamber.

To determine the protein and mineral metabolism it is necessary to collect the urine quantitatively, which is difficult with boys and almost impossible with infant girls. The baby is strapped in a metabolism frame in such a manner that the thighs are flexed and the hips immobilized. The buttocks are thus held over a dish to receive the feces and a glass tube over the penis serves to collect the urine. In experiments on the mineral metabolism long periods should be employed.

Dog Experiments.—In all dog experiments it is necessary to select a healthy animal which can be well trained. For careful work on nitrogen elimination bitches must be used since they can be catheterized at regular intervals. Gross errors are often introduced if dogs void in cages. For respiration experiments the animals must be taught to lie motionless for hours at a time. Many animal experiments have been ruined by restlessness, which introduces a huge error in the results.

Interpretation of Results.—The general reader should bear in mind certain principles in the interpretation of the results of metabolism experiments and not trust entirely to the conclusions of the writers. In the first place he should consider the percentage errors of the methods used, since the error of the total figure may be as great as the error of the least reliable factor. There are exceedingly few methods in which the error is less than 1 per cent.; in many the error is 5 per cent. or more. This shows the futility of expressing results in more than three significant figures. It is important also to bear in mind the number of experiments made and the number of individuals tested, as certain subjects show a rather wide divergence from the normal average and other subjects on certain days diverge from their own average. Short periods of observation must be distrusted, particularly in work on the weight- or nitrogen balance or mineral metabolism.

One of the most frequent sources of error is due to the general impression that the food given to an animal or man represents the food metabolized

[1] Murlin, J. R.: Barker's *Endocrinology and Metabolism*, III, D. Appleton & Co., New York, 1922, p. 627; Murlin, J. R.: *Abt System of Pediatrics.*

This is not due particularly to any deficiency of absorption but rather to the storage of certain foods in the body or loss of food from the body stores. There is almost always some storage after meals with compensatory loss later. A large storage may occur during long periods of overnutrition and a large loss during undernutrition. This introduces a factor of great importance, particularly in work on diabetes.

The reader should familiarize himself with statistical methods and the forms used for graphic representation. In reading a graph it is important to locate the position of the base line for each curve, since many writers, to save space, neglect to follow the general rule of giving the base line in every curve. Sometimes two superimposed curves are made on entirely different scales, thus distorting the facts. In recent years some investigators have been employing for metabolism work the correlation coëfficients which have found wide application in biometry. This is confusing for all except the few readers who have been trained in this somewhat complicated form of methematical expression. While the method is exceedingly valuable in some branches of biological work in which large numbers of observations are made, it is of questionable accuracy in all clinical tests. The correlation coëfficient magnifies the importance of any one experiment which differs greatly from the mean. In clinical work we should perhaps minimize the importance of one great divergence which may be due to the presence of some pathological factor unrecognized by the observer.

FASTING

Although the clinician seldom sees persons who have undergone long periods of complete starvation, he frequently observes the results of profound undernutrition. Moderate undernutrition is practically universal in all patients who are seriously ill, and the metabolic phenomena of fasting are superimposed upon the phenomena belonging to the disease itself.

Water Starvation.[1]—This presents a picture of grave import. While not infrequent in certain diseases, such as intestinal obstruction, œsophageal obstruction, etc., it cannot be studied experimentally in human subjects as, once recognized, it must be relieved by the introduction of fluids. Disasters at sea or in a desert have given rise to harrowing descriptions of the phenomena of water deprivation, but no metabolic studies were possible. A few necessary experiments have been made on animals. Rubner found that starving pigeons die in four to five days, while those allowed water but no food live twice as long. Straub, who gave dogs dried meat and fat, found that the muscles lost 20 per cent. of their water. The living organism gives off water continually through the vaporization from skin and lungs. A definite amount of water is also required for the solution of the urea resulting from the protein metabolism. A constant drain from the body without replacement is offset only in small part by water resulting from the oxidation of body foodstuffs; the greater portions come from the withdrawal of water stored in the

[1] Rowntree, L. G.: *Physiol. Rev.*, 1922, **2**, 116.

tissues and blood. When these stores have been seriously diminished there is a concentration of the blood and a serious diminution in the water content of the cells. We may assume also a retention of metabolic products due to a lack of urinary secretion and it is quite possible that such a retention may be more disastrous in dried tissues. I do not know of any work on this except in cases of cholera in which the rapid loss of water is accompanied by uremic manifestations.

Balcar, Sansum, and Woodyatt[1] injected strong glucose solutions into the veins of dogs and produced a marked diuresis with consequent dehydration of the tissues and later convulsions. High fever resulted and in one animal the temperature rose to 125.6° F. This is the extreme picture of sudden loss of water. The opposite condition of *water intoxication* has been produced by Rowntree, who first gave dogs an extract of the posterior lobe of the pituitary gland, which prevents diuresis and then administered large quantities of water. The symptoms were asthenia, nausea, diarrhœa, ataxia, convulsions, and finally coma.

Food Starvation.—There are many individuals who willingly fast long periods if allowed sufficient water. Some fast in order to obtain publicity, others because they believe that fasting will benefit their health. Many of these "hunger artists" have lent themselves as subjects for scientific investigation. The most famous are Succi, Cetti, and Levanzin. Well authenticated fasts of thirty or forty days are not infrequent. Dogs have fasted from ninety-eight to one hundred and seventeen days. Reptiles can fast for much longer periods. As a rule, the hunger pains are troublesome for a few days only, and after that the discomfort is due chiefly to general weakness and depression. Some professional fasters are able to do a considerable amount of work. There is, of course, a great loss of weight due to the disappearance of water, fat, and muscular tissue. The general health does not seem to be impaired and, if reasonable precautions are taken when food is resumed, there is a rapid gain in weight and strength. Many say that their general health is greatly improved. In recent years some patients with epilepsy have been apparently benefited by fasting two or three weeks.

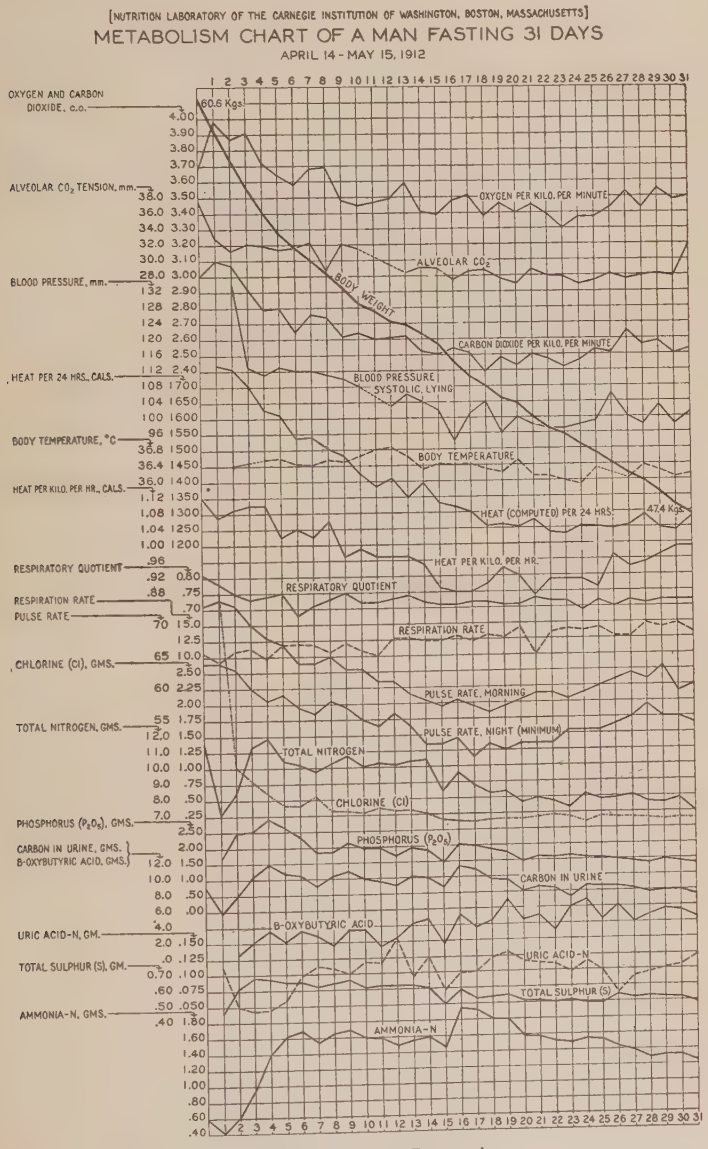
In a consideration of the metabolic phenomena we may skip the early work, important though it is, and concentrate our attention upon the classical experiment of F. G. Benedict,[2] who secured as a subject a Maltese pharmacist, named Levanzin. He had previously undergone several fasts in Malta and came to Boston to be studied in the calorimeter of the Nutrition Laboratory. After a short preliminary observation he began a fast of thirty-one days, receiving nothing but water. He was under constant observation. At night he slept in the bed calorimeter and during the day his respiratory metabolism was determined by the "Unit Apparatus." Many other physical and psychological tests were made. The results are shown in Fig. 2. His body weight dropped rapidly from 60.6 kilograms to 47.4 kilograms, a loss of 21.9 per cent. of the original body mass. A study of the respiratory quotient enables us to ascer-

[1] *Arch. Int. Med.*, 1919, **24**, 116.

[2] *A Study of Prolonged Fasting, Carnegie Institution of Washington*, Pub. No. 203, 1915.

tain the rate at which the stored carbohydrate was utilized. On the first day he oxidized 69 gm. of glycogen, on the second and third days about 40 gm. a day, after that about 4 gm. a day until the thirteenth, from which

FIG. 2



Benedict's subject, Levanzin.

time on there was no evidence of the combustion of carbohydrate as such, and all the calories were furnished by fat and protein. We must remember that the protein molecule contains substances which give rise

to glucose and we cannot therefore say that carbohydrate metabolism ceased or that the glycogen stores in the body were completely exhausted.

The protein metabolism during fasting is particularly interesting. Levanzin on the day before his fast excreted 11.5 gm of nitrogen in the urine. This fell to 7 to 8 gm. during the first two days of the fast representing the metabolism of 44 to 50 gm. of protein. After the third day the nitrogen elimination rose, probably because the glycogen stores had been diminished. In the latter half of the fast, the protein metabolism fell once more, probably because of the great reduction in total metabolism.

Levanzin's protein metabolism was somewhat higher than that usually found in other subjects, but it followed the general rule of falling in the first two days and then rising as the sparing action of carbohydrate diminished. We shall see in another place that the level of protein metabolism is influenced by the proportion of calories derived from carbohydrate food. With an abundance of carbohydrates in the diet it is possible to secure a protein minimum with an excretion of 2 to 3 gm. of nitrogen a day, figures much lower than those found in complete starvation. A nitrogen excretion of 7 to 8 gm. a day, such as we find in starvation, is about the same as when a man is given over a considerable period a diet consisting entirely of fat. The fat in the diet then merely takes the place of the body fat utilized by the fasting man. It is perhaps well to remind the reader that the total loss of nitrogen in a normal fasting man (7 to 8 gm. a day) is much less than that frequently encountered in fever patients, who sometimes show a negative balance of 10 to 20 gm. a day when they are on ordinary fever diets with an intake of 5 to 10 gm. of nitrogen. In such fever patients we often encounter a toxic destruction of protein. This may also be found in carcinoma and perhaps in other cachexias.

In the case of Levanzin protein furnished between 14 and 19 per cent. of the total calories. It is interesting to see how this corresponds to the percentage of calories obtained in fasting experiments on various animals. Lusk has given such a table which demonstrates the uniformity of this percentage in spite of the great variation in weight of the animals and differences in total metabolism and actual level of nitrogen excretion. This table illustrates the importance of considering the percentages of the various foodstuffs oxidized. Protein supplies 10 to 15 per cent. and in the case of Levanzin and starving animals the remaining calories are furnished by fat after the first few days, which exhaust the glycogen stores.

TABLE 2.

Animal.	Weight, kg.	Percentage of calories from protein.
Pig	115.0	7.3
Man	63.7	15.6
Dog I	28.6	13.2
Dog II	18.7	10.7
Dog III	7.2	13.5
Rabbit	2.7	16.5
Goose	3.3	7.4
Fowl	2.1	10.0
Guinea-pig	0.6	10.8

In another place the question of *ketosis* is discussed in greater detail. The molecule of fat is not completely broken down to water and carbon dioxide unless at the same time a molecule of glucose is also oxidized. Some of the fatty acid does not go beyond the stage of beta-hydroxy-butyric acid or diacetic acid and the organism excretes these and acetone in the urine. It is not therefore surprising that in the case of Levanzin the ketones made their appearance on the second day of the fast and thereafter fluctuated between 1.4 and 7.0 gm. per day calculated in terms of total beta-hydroxy-butyric acid. This amount would have been much greater were it not for the fact that the protein furnished from its molecule a considerable amount of glucose. It is quite possible that the relatively high protein metabolism of Levanzin accounts for the fact that his ketosis was less marked than in certain other fasting subjects. Brugsch found with Succi 8.4 to 13.6 gm. of beta-hydroxy-butyric acid between the twenty-third and thirtieth days of starvation. Grafe reports 15 to 16 gm. of acetone bodies in the third week of starvation. Such a ketosis, though important, is not menacing and does not compare with the figures in severe diabetes because in diabetes the glucose from the protein is excreted and, therefore, cannot be utilized by the body in completing the metabolism of the fatty acids. In both diabetes and fasting the essential cause of the ketosis is a lack of available carbohydrate. It is not therefore surprising that we find acetone bodies in the urine quite frequently in undernourished patients with various diseases and more particularly in babies.

In any patient in whom the total available glucose obtainable from the food glycogen stores, and protein metabolism falls below a certain level in relationship to the fat metabolized, there will be incomplete oxidation of the fatty acids. These in themselves are not often threatening, but they represent a waste of good calories and show us that the carbohydrate metabolism has fallen to a point which will inevitably lead to a greater destruction of body protein. In such a case the administration of moderate amounts of carbohydrate not only furnish calories but insure the better utilization of fats and also the sparing of body protein.

Basal Metabolism in Fasting.—On the first day of the fast Levanzin's basal metabolism calculated for twenty-four hours (average of direct and indirect measurements in the calorimeter), was 1432 calories. This level of heat production fell quite rapidly, reaching 1002 calories on the twenty-first day, then rose a little on the last days of the fast. Part of this fall was of course due to the loss in body substance, but Benedict calculating the calories per kilogram of body weight per hour, found 1.07 in the first day, 0.87 on the twenty-first, and 0.99 on the thirty-first day. According to the surface area the figures were as follows: 904 calories per square meter per twenty-four hours on the first day, 664 on the twenty-first day, 737 on the thirty-first day.

Lusk calculated that Levanzin's body had lost about 11.2 per cent. of its total protein by the twenty-first day. The percentage fall in metabolism was distinctly greater than this figure, indicating some factor as yet unknown which tends to diminish the needs of the body during continued starvation. This same phenomenon has been found in many

other starving subjects. It is perhaps most striking in starving diabetic patients, and in these the diminished demand for calories is of great help in allowing us to meet the diminished power to oxidize glucose.

Chronic Inanition.[1]—The various phenomena demonstrated by complete starvation are reproduced to a lesser degree in partial starvation. Almost all patients who are seriously ill are undernourished. This is due not only to loss of appetite and restricted diet, but also in most diseases to an increase in the basal metabolism. Short periods of low diets, as in an attack of tonsillitis, probably do not appreciably affect the metabolism, certainly not as much as do the fever and toxemia. In fevers of longer duration and in all chronic illness the relative undernutrition is often striking. Clinicians are familiar with the marked losses in weight, though sometimes this is masked by retention of water, with visible or invisible œdema. The nitrogen elimination is usually dependent upon the degree of toxemia, so it is influenced greatly by the amount of carbohydrate in the diet. The fat metabolism and ketosis have been discussed in the previous paragraph. The basal metabolism always tends to fall as a result of undernutrition, but this tendency is usually more than counterbalanced by the increase due to the disease itself. The total metabolism depends not only on the basal, but also on the activity of the patient.

Svenson in 1901 showed that in certain emaciated typhoid convalescents the basal metabolism was exceedingly low. Magnus-Levy in 1906 called attention to the profound alteration in basal metabolism caused by undernutrition. A young barber entered his hospital greatly emaciated. He was of neurasthenic disposition and in an effort to cure his constipation, had lived for nine months on a ridiculously low diet of 700 to 800 calories a day. Magnus-Levy continued this ration for a few days and found his metabolism 33 per cent. below normal. On a liberal diet the heat production rose rapidly, later going somewhat above the average normal during the lighting-up of a pulmonary tuberculosis. When this attack subsided his metabolism was found to be normal. The figures are given in Table 3.

TABLE 3.—METABOLISM EXPERIMENT ON MAGNUS-LEVY'S PATIENT.*

Period.	Date.	Condition.	Calories per sq. m. per hour, height-weight formula.	Weight, kg.	Relationship of metabolism to average normal 39.7 per cent.
I . .	Nov. 16 to 21	Very low diet	26.6	36.2	−33
II . .	Nov. 23 to Dec. 9	Liberal diet	33.0	38.0	−17
III . .	Jan. 26 to Mar. 6	Fever from tb.	43.4	48.4	+ 9
IV . .	Mar. 13 to May 8	Normal again	40.5	52.2	+ 2

* Age, nineteen years; height, 160 cm.

Allen and Du Bois in 1916 found a similar reduction in a large series of emaciated diabetic patients and called attention to its clinical significance.

[1] Lusk, G.: *Physiol. Rev.*, 1921, 1, 523.

Benedict's Studies on Students.—During the Great War the problems of chronic undernutrition assumed world-wide importance. Benedict, Miles, Roth, and Smith[1] at this time undertook an elaborate study, using as subjects groups of volunteers from the Y. M. C. A. training school in Springfield, Mass. These young men were all athletic and extremely conscientious in their diets. One group of twelve (Squad A) before the experiment began were taking 3200 to 3600 net calories a day, then for three weeks they were given only 1400 calories a day without reducing their physical or mental work. At the end of this period their weight had fallen 12 per cent. and they were able to maintain this weight and continue their work when the diet was increased to the low level of 1950 calories, a figure which was about one-half of the original intake. The heat production measured during sleep fell to about three-quarters of its original level, the diminution per square meter of body surface being about 18 per cent. With the fall in weight the bodies lost on an average 150 gm. of nitrogen. Systolic and diastolic blood-pressures fell, the pulse-rate was slow, in some cases reaching 33 per minute. Temperature was unaffected. On account of the loss in weight the subjects were able to walk a mile with a lower expenditure of energy than before the experiment. The loss of body strength was not marked, but the men suffered from the cold, they lacked initiative and energy, and there was a marked diminution in sex expression. All these same phenomena have been observed in undernourished populations during the war. Lusk has made a careful analysis of the results of the experiments on Squad B, a control group which was later placed on a low diet for three weeks. In this second group a reduction of 6.5 per cent. in body weight and 3.2 per cent. in body nitrogen was accompanied by a diminution of 27 per cent. in calories per square meter of body surface.

It is rather surprising that the organism can stand undernutrition without loss of muscular efficiency. Anderson and Lusk studied the heat production of a dog running on a treadmill at the rate of 3 miles an hour. When the animal was well fed it required 0.550 kilogram-meters of energy to move 1 kilo of body weight 1 meter. After thirteen days of fasting, with a loss of 20 per cent. in body weight it required 0.584 kilogram-meters a change which is insignificant.

THE MIXTURES OF FOODSTUFFS OXIDIZED

In all discussions of metabolism it is necessary to consider the proportions in which the various foodstuffs are metabolized. Carbohydrate, fat, and protein are all more or less interchangeable as sources of heat. The percentage of calories furnished by each one depends directly upon the two others. To represent these facts graphically the writer[2] constructed triangles which resemble somewhat those used by Irving Fisher to show the composition of foods. In Fig. 3 the lower left-hand corner of the triangle represents a point where all of the calories are supposed

[1] *Human Activity and Efficiency under Restricted Diet, Carnegie Institution of Washington*, Pub. No. 280, 1919.

[2] Du Bois, E. F.: *Jour. Biol. Chem.*, 1924, **59**, 43.

to be derived from fat; the lower right-hand corner represents 100 per cent. of the calories from carbohydrate; the top of the triangle represents protein. Of course, it is impossible for the organism to derive all of its calories from any one of these three foodstuffs, but we may use these as the boundaries of the metabolism map. A set of diagonal rulings starting on the left side of the triangle and running parallel with this toward the carbohydrate corner shows us the positions which indicate that 10, 20, 30, etc., per cent. are derived from this latter source. A similar set of horizontal lines, starting at the base and progressing upward, show the points on which protein furnishes 20, 40, 60 per cent. of the calories. Thus we can find for any point in the triangle the percentage of calories derived from carbohydrate and the percentage from protein. Adding these, it is easy to calculate the percentage from fat, which is the only other source of energy.

Fig. 3

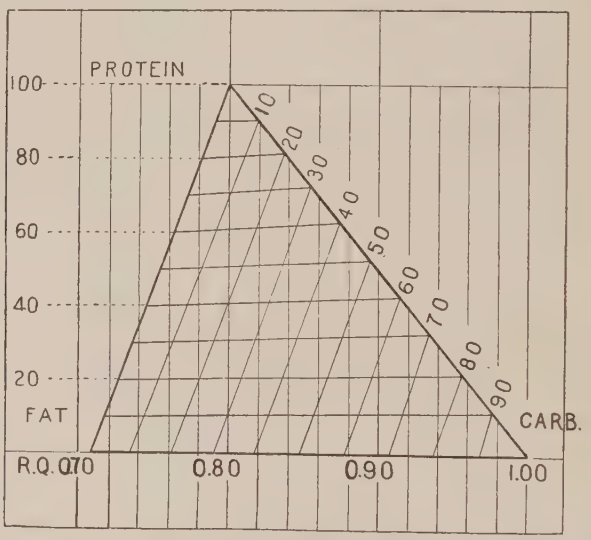


Diagram showing the percentages of calories derived from protein, fat and carbohydrate according to the respiratory quotient. The base line gives the total respiratory quotient; the ordinates reading on the left-hand side give the percentage of calories from protein; the diagonals reading on the right of the triangle give the percentage from carbohydrate.

In order to familiarize ourselves with the diagrams let us consider three widely different dietaries, those of Europeans (Voit's standard), Bengalis, and Eskimos.[1] If we calculate in Table 4 the percentages of calories furnished by each of the three we can readily find their positions on the triangle, Fig. 3. The larger the proportion of carbohydrate the closer will the point come to the right-hand corner; the greater the protein ration, the nearer the apex. A diet having nothing but fat would come close to the lower left-hand corner.

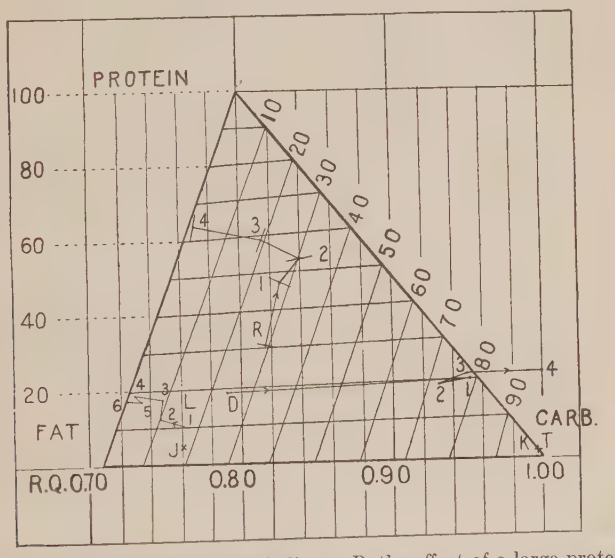
[1] Lusk, G.: *The Fundamental Basis of Nutrition*, 2d ed., Yale University Press, New Haven, 1923.

TABLE 4.

Diet.	Protein, grams.	Total calories.	Percentage of calories from. Protein.	Fat.	Carbohydrate.
European (Voit's)	118	3055	16	17	67
Eskimo	282	2604	44	48	8
Bengali	52	2390	9	10	81

This triangle was constructed on a base line which represents the respiratory quotient. The carbohydrate corner was placed at 1.00, the fat at 0.707, and the apex for protein over 0.801. The diagonals were calculated according to a rather complex mathematical formula and they are not quite evenly spaced. The inclusion of the respiratory quotient in the diagram makes it possible to place all the experiments in the literature which give the respiratory quotients and the percentage of calories furnished by protein. If the authors do not give the data for the protein metabolism we may assume for most basal experiments that this will furnish from 10 to 20 per cent. of the calories.

FIG. 4



Triangles used to show changes in metabolism. *R*, the effect of a large protein meal; *D*, the effect of 200 gm. of glucose; *L*, the first six days of starvation; *KT* and *J*, low-protein diets with muscular exercise.

In all the publications on clinical calorimetry from the Russell Sage Institute of Pathology there are tables showing the percentages of calories derived from protein, fat, and carbohydrate. Up to 1924 these contain an error of 2 or 3 per cent. in the apportionment between carbohydrate and fat, due to the employment of a table which was slightly inaccurate. The error fortunately is not great enough to change the significance of any of the results, and we can therefore plot the calorimeter experiments directly on our triangular metabolism maps. This has been done in the

case of several striking experiments in Fig.4. The upper curve represents the changes in the metabolism of a muscular achondroplastic dwarf, R. de P., after the consumption of a breakfast of 662 gm. of chopped beef, which was relatively enormous for a dwarf weighing 90 pounds. The starting point *R* gives the position of his basal metabolism the day before the experiment. The point 1 represents the position reached in the period which started one hour after he had finished the breakfast, which contained 23.2 gm. of nitrogen. Numbers 2, 3, and 4 show the results of the next three hours. It will be noted at the end of the fourth hour that he was deriving 64 per cent. of his calories from protein, perhaps the largest amount yet demonstrated in a respiration experiment in man. Carbohydrate as such furnished only 2 per cent. of the calories, and the remaining 34 per cent. must have been derived from fat. An attempt has been made in this curve to represent the changes in the total calories by drawing cross lines whose lengths are proportional to the heat production each hour. This shows graphically the effect of the specific dynamic action of protein, which raised the metabolism from its original basal level of 52 calories an hour to 78 to 80 calories in the last three hours.

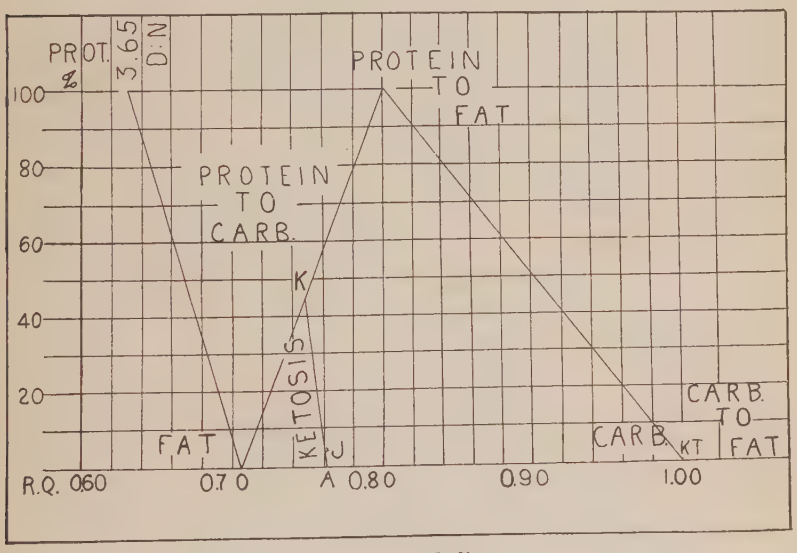
On this same figure *D* represents the usual position of the basal metabolism of one of the normal controls. In a certain calorimeter experiment he was given 200 gm. of dextrose on an empty stomach. The figure 1 on this line shows his metabolism in the sixty-minute period which began one hour after he had taken the sugar. For the next two hours the calories were derived almost exclusively from protein and carbohydrate. In the fourth hour the line passed outside of the triangle, indicating that some of the carbohydrate ingested was being transformed into fat.

The line starting at *L* is taken from the work of F. G. Benedict on the fasting subject Levanzin. The numbers represent the first six days of starvation. By the sixth day practically all the available carbohydrate had been exhausted and he was on an exclusively protein-fat basis. The point *J* represents the metabolism of a man studied by Atwater and Benedict who expended 9981 calories in a single work day while he was on a diet containing 5138 calories. This represents the fact that muscular work may be performed through the oxidation of food and body fat with an exceedingly low level of protein metabolism. The point *KT* gives the figure for a similar work experiment by Karl Thomas on a diet low in nitrogen and rich in carbohydrate. Only 1.5 per cent. of the calories were derived from protein.

It will be noted that on this map there is a narrow zone at the bottom and a wide area at the top which can never be traversed by the metabolism of man, since it is difficult to conceive of a condition in which he derives less than 1 per cent. or more than 70 per cent. of his calories from protein. On the other hand, there are certain positions outside the triangle which can be reached, as is shown in Fig. 5. We have already seen that carbohydrate can be transformed into fat when the respiratory quotient is high. The transformation of protein to fat has been noted in respiration experiments on dogs, but not yet on human subjects. In

diabetes mellitus or phlorhizin glycosuria the respiratory quotient may be below 0.707, and there is, therefore, a zone to the left of the triangle in which the carbohydrate portion of the protein molecule is excreted in the urine instead of being utilized. It is only the lower part of this inverted triangle that is reached by man since rarely even in severe diabetes do we find that more than 40 to 50 per cent. of the calories are derived from protein. The line *KA* in Fig. 5 represents the threshold of ketosis. To the left of this line is the zone in which the glucose derived from carbohydrate and protein is insufficient to secure the complete oxidation of the fatty acids from fat and protein. The farther to the left of this line the greater is the ketosis. It will be noted that there is no theoretical ketosis on a pure protein-fat ration if protein furnishes more than 44 per cent. of the total calories. These triangles are discussed at some length in order that the clinician may visualize the metabolism of

Fig. 5



Zones of metabolism.

the individual under his care. He can, for instance, picture the typhoid patient with a high-protein metabolism drifting off to the left of the chart unless he is given large amounts of carbohydrate, which tend to put him back to the normal zone of lower-protein metabolism, with at least one-quarter of the calories being derived from carbohydrate. He may visualize the reparative processes in typhoid convalescence, in which ingested fat is stored as such and some of the ingested carbohydrate is transformed to fat. The application to diabetes is quite obvious, and the practitioner must strive to maintain his patient on the right side of the line which represents the threshold of ketosis.

THE CARBOHYDRATES[1]

The carbohydrates are formed chiefly by the action of sunlight on the leaves of plants. They are compounds of carbon, hydrogen, and oxygen, the formula for glucose, a typical member of the group, being $C_6H_{12}O_6$. Practically all the carbohydrates contain their hydrogen and oxygen in the same proportion as water, H_2O, but we must not forget that there are other substances, such as lactic acid and acetic acid, which contain these elements in the same proportions. Pure carbohydrates are white; most of them crystallize some like starch, are colloidal. Some of the simpler carbohydrates contain in their molecule the aldehyde group, others contain the ketone group, and we may therefore divide them into aldoses and ketoses. These carbohydrates oxidize readily and therefore act as reducing agents.

Carbohydrates are divided according to the number of saccharide (simple carbohydrate) groups contained in the molecule. The following table, from Matthews, shows the various divisions and gives the important representatives of each group. It will be noted that the disaccharides break down to monosaccharides, cane sugar for instance forming glucose and levulose.

Monosaccharides.—Of the monosaccharides the *hexoses* alone are of importance as foods. These have the formula $C_6H_{12}O_6$. The *aldoses* and *ketoses* differ from each other in the arrangement of the hydrogen and oxygen groups in their structural formulas. The aldoses differ among themselves in the forms of their molecules, and the reader who is interested in this subject should look up the fundamental discoveries of Pasteur, who as a young man laid the foundation of our knowledge of the different forms of crystals. Two chemicals may have the same structural formula, yet differ in their properties on account of the different shape of their crystals. The crystal of one is very often the mirror image of the other and as a result the two may act quite differently in rotating a plane of polarized light. *Dextrose* (d-glucose), or grape sugar, is the most important monosaccharide in the metabolism of animals. It is found in the sap of most plants and in the juice of many fruits, but for commercial purposes it is usually obtained through the action of dilute acids on starch. Ordinary *glucose* is a mixture of two varieties, the A and B. In fresh solutions only the A variety exists and this is slowly transformed into the B variety, which has a greater rotatory power on a plane of polarized light. In the presence of alkalis, even though very weak, this change takes place rapidly. Glucose is readily fermented by the enzyme of yeast, zymase. *d-Lævulose* (d-fructose) is widespread in Nature and is even sweeter than glucose. Like glucose, it is fermentable by yeast and reduces solutions of copper salts, but differs from it in being levo-rotatory. *d-Galactose* is one of the constituents of the disaccharide lactose and is also found in the seeds of certain plants.

[1] For details consult Matthews, A. P.: *Physiological Chemistry*, 3d ed., Wm. Wood & Co., New York, 1921; Hawk, P. B.: *Practical Physiological Chemistry*, 8th ed., Blakiston's Son & Co., Philadelphia, 1923.

TABLE 5

- **Carbohydrates**
  - **I. Monosaccharides**
    - 1. Bioses. — Aldose. *Glycolaldehyde.*
    - 2. Trioses. — Aldoses. *Glycerose.* / Ketoses. *Dioxyacetone.*
    - 3. Tetroses. — Aldoses. *Erythrose.* / Ketoses. *d-Erythrulose.*
    - 4. Pentoses. — Aldoses. *Arabinose, xylose, ribose.* / Ketoses. *l-Arabinulose.*
    - 5. Hexoses. — Aldoses. *Dextrose, galactose, mannose.* / Ketoses. *Levulose, sorbose.*
    - 6. Heptoses. — Aldoses. *d-Mannoheptose.*
  - **II. Disaccharides**
    - 1. Lactose. — (Glucose + galactose.)
    - 2. Maltose. — (Glucose + glucose.)
    - 3. Saccharose. — (Glucose + levulose.)
    - 4. Trehalose. — (Glucose + glucose.)
    - 5. Melibiose. — (Galactose + glucose.)
  - **III. Polysaccharides**
    - 1. Trisaccharides. — *Melitose* (Raffinose) in molasses. / *Melizitose.* (Pinus larix.) (Levulose + glucose + galactose.)
    - 2. Tetrasaccharides. — *Lupeose* in peas; *stachyose,* (Lupeose consists of 2 molecules of galactose, 1 of glucose, and 1 of levulose.)
    - 3. Colloidal polysaccharides. — *Dextrins.* / *Glycogen.* / *Cellulose.* / *Starch.* / *Mucilages.* / *Gums.* / *Inulin.*

It is interesting in this connection to note that the glucosides, which form the active principles of many important drugs, liberate sugar, usually glucose, when hydrolyzed with acids. A glucoside is an ether of glucose, or some other sugar, and an alcohol.

Disaccharides. The hexose disaccharides have the formula $C_{12}H_{22}O_{11}$, and when they are hydrolyzed by the addition of H_2O to the molecule yield two molecules of monosaccharides, as indicated in the table above. *Saccharose* (sucrose, cane sugar, beet sugar) is found in beets, sugar cane, and sap of maples, etc. On hydrolysis it yields dextrose and levulose. It reduces Fehling's solution very slowly. It is inverted, changed into a mixture of glucose and levulose by acids or by certain enzymes found in yeast, plants and in intestinal secretions of mammals.

Lactose.—Lactose, $C_{12}H_{22}O_{11} + H_2O$, is the sugar of milk formed by the mammary glands. When hydrolyzed by acids or by the enzyme lactase, found in the intestinal mucosa, it yields galactose and glucose. It is not fermented by yeast, but is fermented by the bacillus coli communis and several other intestinal organisms. Lactose is sometimes found in the urine and is confused with glucose because it reduces Fehling's solution readily. It can be distinguished from glucose, since it is not fermentable by yeast. Lactose is excreted by the kidney quantitatively if it finds its way into the blood from a mammary gland or if it is introduced under the skin or into a vein. This is due to the fact that the body contains no lactase except in the alimentary tract, and the disaccharide cannot be oxidized until it has been broken down into glucose or galactose.

Maltose.—Maltose is found in germinating barley and is readily formed by the action of amylase on starch. It is therefore very common in animal and plant tissues, since both starch and the enzyme are found in almost all animals and plants. Maltose reduces Fehling's solution and ferments with yeast. We are not sure as to whether or not the animal tissues can utilize it directly before it is changed to glucose.

Polysaccharides.—Living tissues are able to form polysaccharides from monosaccharides possibly by means of a simple dehydration. Starch or amylum $(C_6H_{10}O_5)_n$, the most important of the polysaccharides, yields glucose when hydrolyzed with acids. Wheat flour, which is chiefly starch, contains a small amount of amylase. When mixed with water and yeast the amylase attacks the starch, setting free maltose which is then fermented. The yeast itself contains no amylase. The gastro-intestinal tract of man, however, contains an abundance of this ferment, and starch is broken down to glucose, which is then absorbed.

Glycogen.—Glycogen is the polysaccharide contained in the animal body, human muscle containing about 0.5 per cent. and human liver a much higher percentage. Schöndorff found 18.7 per cent. of glycogen in the liver of dogs. This carbohydrate is also found in scallops and oysters. Glycogen possesses some of the properties of starch and dextrin. Apparently, the glycogen stores of the body are transformed into glucose as needed and this in turn into lactic acid, furnishing muscular energy. It is difficult to study the glycogen content of animal tissues, since they contain enzymes which break down the glycogen quite rapidly after death.

Cellulose.—Cellulose is a polysaccharide which forms the main constituent of the walls of plant cells. It cannot be utilized by the human intestinal tract, but can be made to yield glucose and other monosaccharides by hydrolysis with acids.

DIGESTION OF CARBOHYDRATES

The monosaccharide and disaccharides probably pass to the intestine practically unchanged by the salivary and gastric secretions. Polysaccharides, however, are acted upon by the ptyalin, the amylase of saliva, which hydrolyzes starch. We do not know the exact steps of the process, but we can recognize the formation of various simpler dextrines with the splitting off of maltoses. This maltose passes on to the intestine, though perhaps a small amount is converted into glucose by the maltase found in saliva. Ptyalin is most active in a very faintly acid solution and continues in the stomach to digest some of the starch until the hydrochloric acid permeates the mass of food in the fundus.

The juice secreted by the duodenal mucosa contains, in addition to enterokinase, the carbohydrate enzymes, invertin, maltase, and lactase, which convert cane sugar, maltose and lactose, respectively, into monosaccharides.

The pancreatic secretion contains a powerful enzyme, amylopsin, which acts upon starch and glycogen, converting them into maltose. The pancreatic juice of young animals and man also contains lactase, the enzyme which splits milk sugar into glucose and galactose. This ferment persists into adult life in the case of man. Maltase, which converts maltose into glucose, is also present in the pancreatic secretion.

We see a constant breaking down of all the carbohydrates until they reach the simple stage of glucose or levulose or galactose. These may be absorbed by the intestinal tract and passed into the blood. Here they may be oxidized or may be converted into glycogen. Glucose, which is the chief sugar of the blood, readily forms glycogen through dehydration.

The intermediary metabolism of the sugars is still somewhat problematical. During the contraction phase of muscle, glycogen is converted into glucose and this breaks down into lactic acid, furnishing the energy for the work performed. During the recovery phase this lactic acid is built up again into glucose through the agency of energy furnished by the oxidation of glucose or fat. The trioses, glyceric aldehyde and methylglyoxal, may be intermediary steps in the oxidation of the sugars. Whatever the intermediary steps, the oxidation results in the formation of carbon dioxide and water.

$$C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O.$$

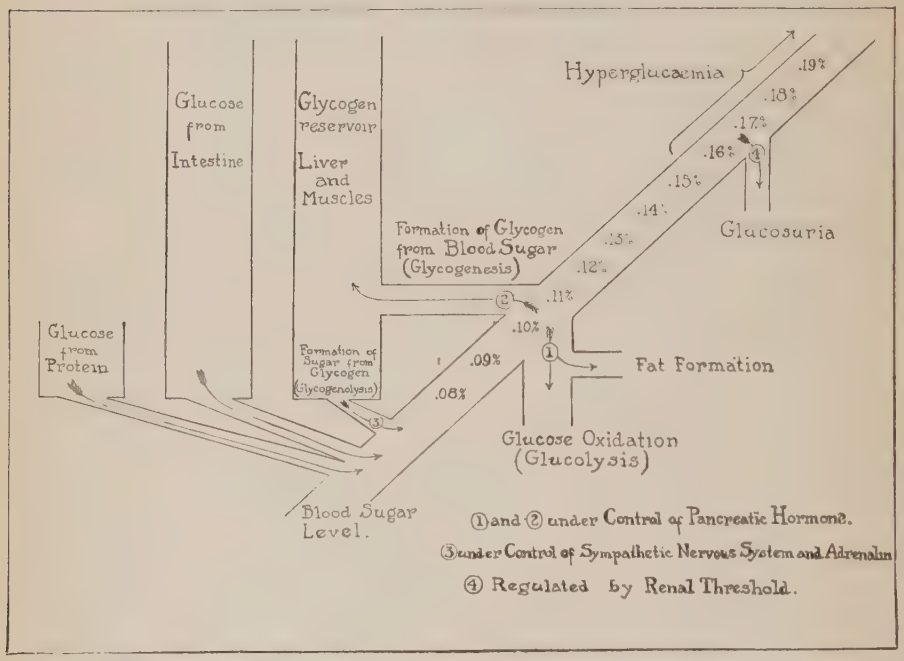
We have already seen that this chemical equation furnishes us with a method of determining the amount of carbohydrate oxidized provided we can measure the oxygen consumed and the carbon dioxide produced.

Since the monosaccharides are readily soluble they are completely absorbed by the intestinal tract unless there is exceptional diarrhœa. The disaccharides are readily broken down into the monosaccharides and are completely absorbed also. Some of the sugars which have escaped

absorption in the upper intestine may be fermented by bacteria in the lower intestine, thus producing the gases, carbon dioxide, hydrogen, methane and other substances, such as lactic acid and alcohol, which are absorbed and oxidized.

In certain rough or poorly cooked foods the digestive juices are unable to reach all of the carbohydrate, chiefly starches, contained in the vegetable fibres. Under such conditions some of the carbohydrate escapes absorption and fermentation and is excreted in the feces. The human intestinal canal is usually able to absorb enormous amounts of carbohydrates with an almost negligible percentage loss in the stools.

FIG. 6



Schematic illustration of the factors which regulate the sugar concentration of the blood. (Ringer and Baumann.)

Blood Sugar.—The cells of the body are continually bathed in a weak solution of glucose. The blood usually contains about 0.1 per cent. of glucose and the tissue fluids apparently about the same concentration, although we have not very much data on this subject. The muscles apparently contain about one-half this amount. This supply is renewed either from the food absorbed or from the glycogen stored in the liver. It seems as though there were rather large variations in the amount of glycogen thus stored, and estimates of the total carbohydrate depots vary between 100 and 400 gm. S. R. Benedict has shown that the normal kidney excretes about 1 gm. of carbohydrate a day, the concentration of this substance in the urine being so small that it does not react with the ordinary methods for determining sugar. When, however, the sugar of

the blood rises above 0.16 to 0.18 per cent., the so-called normal renal threshold, some of the sugar is excreted. In diabetes and nephritis and several other conditions, this threshold may be very much higher. We must remember also that the rate of disappearance of the sugar from the blood is dependent largely on the total need for fuel by the body, and this depends upon the size of the individual, the muscular activity, and other factors which influence the total metabolism. It also depends upon the rate at which glucose is withdrawn for storage in the liver and for transformation into fat, such a transformation, for example being extremely active in convalescence from wasting fevers. Ringer and Baumann[1] have expressed the various factors most beautifully in the diagram which is reproduced.

The *glucose tolerance* test is of considerable service in diagnosis. A stated amount of glucose, usually 100 gm,. is given on an empty stomach and the level of blood sugar determined at half-hour intervals until it has fallen approximately to its original level. Individuals who weigh less than 60 kilograms are usually given smaller amounts, but it is somewhat illogical to base the dosage strictly on weight. A more rational method would be to give an amount of glucose with a caloric content a certain percentage above the basal metabolism. Fitz has shown that there are great variations in the speed with which such glucose is absorbed. A consideration of the various other factors shown in the diagram makes us rather cautious in our evaluation of the significance of variations in the shape and level of the blood-sugar curve. It is, nevertheless, of importance to recognize the fact that in most normal individuals after the ingestion of 100 gm. of glucuse, the blood sugar fails to reach a point above 1.5 per cent. and starts to fall by the end of the second hour. A more exact method of testing the ability to oxidize carbohydrate could be developed by making a series of determinations of the respiratory quotient after the ingestion of a suitable amount of glucose. This would be so laborious that it could not be utilized in the clinic. It is not entirely without practical value, however, as the writer was able to prove on one occasion when an exophthalmic goitre patient with glycosuria, was, after the ingestion of 100 gm. of glucose, deriving 89 per cent. of his calories from carbohydrate, the respiratory quotient being 0.98. This proved that there was no interference with the metabolism of sugars. We must remember that the mobilization and oxidation of the sugars are controlled not only by insulin from the pancreas but also by the liver, adrenals, thyroid, pituitary and the sympathetic nervous system.

THE FATS

Fats are widely distributed in animals and plants. They are formed by the fermentative decomposition of the sugar and represent essentially carbohydrates which have lost some of their oxygen and have, therefore, been condensed. Since they retain the carbon and hydrogen which furnish large amounts of heat, they produce gram for gram more than twice as

[1] Barker's *Endocrinology and Metabolism*, D. Appleton & Co., New York, 1923, **3**, 252.

many calories as the original carbohydrate. The oxygen which has been lost through the reduction process is always available in the blood. The fats, therefore, constitute ideal storehouses of energy. They also help to prevent the loss of heat when they are deposited in the subcutaneous tissues.

The fats are merely one subdivision of the great class of lipins, some times called lipoids. There are several classifications but we follow the one suggested by Gies:

Lipins. Constituents of protoplasm having a greasy feel; soluble in alcohol-ether.

1. (*a*) **Fats.**—Neutral esters of glycerol and fatty acids which are solid at 20° C.
   (*b*) **Fatty acids.**
2. **Fatty Oils.**—Neutral esters of glycerol and fatty acids liquid at 20° C.
   A. Drying oils. Harden on exposure to light and air. Linseed oil.
   B. Semi-drying oils. Thicken slowly on exposure to light and air. Cotton-seed oil.
   C. Non-drying oils. Remain liquid on exposure to light and air. Olive oil.
3. **Essential Oils.**—Volatile, generally odoriferous substances of oily and of varied chemical nature, being aldehydes, acids, terpenes, alcohols, etc. Oil of cloves, turpentine, wintergreen, etc.
4. **Waxes.**—Esters of sterols and fatty acids. Beeswax, carnauba wax. Sperm oil. Spermaceti.
5. **Sterols.**—Alcohols, generally of terpene group, solid at ordinary temperatures. Cholesterol, phytosterol, cetyl alcohol, myricyl alcohol, etc. (Oxidation products terpenic acids.)
6. **Phospholipins.**—Phosphatides. Fatty substances yielding on hydrolysis phosphoric acid and fatty acids.
   A. Mono-amino-monophospholipins. Lecithin, cephalin.
   B. Di-amino-monophospholipins.
   C. Mono-amino-diphospholipins.
7. **Glycolipins.**—Fatty substances yielding on hydrolysis fatty acids and a carbohydrate, generally glucose or galactose. Contain no phosphorus. Cerebron. Kerasin. Phrenosin.
8. **Sulpholipins.**—Fatty substances yielding on hydrolysis fatty acids and sulphuric acid. Sulphatide of brain. Protagon. Nature still undetermined.
9. **Aminolipins.**—Fatty substances containing amino-nitrogen and fatty acids. Contain no phosphorus. Not well characterized. Bregenin.

The fats and fatty oils are the neutral esters of the trihydric alcohol glycerol, $C_3H_8O_3$, and some of the higher fatty acids, such as palmitic, $C_{16}H_{32}O_2$, stearic, $C_{18}H_{36}O_2$, oleic, $C_{18}H_{34}O_2$, It will be noted that these fatty acids and, in fact, all the others found in natural food, fats and oils, contain an even number of carbon atoms. They are probably formed by the addition of 2, 4, etc., carbons at a time and are broken down in the same manner. The consistency of the fat at ordinary temperatures

depends upon the fatty acids which it contains. Tripalmitin and tristearin which are the chief constituents of the fats of mammals, are solid at room temperature. Another constituent, triolean, also found in large quantities in olive oil, is fluid at room temperature. It is therefore easy to realize that fatty acids such as these, when mixed in different proportions, melt at very different temperatures. In Nature fats usually occur in mixtures.

Glycerol.—Glycerol (glycerine) is a substance with a sweet taste, closely related to the carbohydrates. It is easy to trace its possible formation from sugar and its possible conversion into sugar. We have as yet no proof that the fatty acids of an even number of carbon atoms can be transformed in the animal body into sugar. Ringer has shown that fats artificially made so as to contain an uneven number of carbon atoms may form sugar instead of ketones in the diabetic organism. Such a fat has been put on the market under the name *Intarvin*.

Some of the drying oils are of interest from the metabolic standpoint, since they have the property of taking up oxygen and giving off carbon dioxide. This spontaneous respiration is accelerated by ultra-violet light and certain salts which are oxidative accelerators.

Of the stearols we are interested chiefly in *cholesterol* or cholesterin. This is the chief constituent of gall-stones and is also present in large amounts in brain tissue. The cortex contains about 1.15 per cent., the white matter 2.47 per cent. It is present also in the blood, and recently has been attracting attention in its relationship to gall-stones, anemia, nephrosis, and several other diseases.

Phospholipins.—Phospholipins are of great importance as constituents of the cells rather than as storehouses of energy. They seem to be one of the essential constituents of living matter. Their name is derived from the fact that they always contain phosphoric acid. They also contain some of the higher fatty acids, most of them glycerol also, and many have an organic base containing nitrogen. The most important of the group are *lecithin* and *choline*. They show the property of auto-oxidation and are extremely active substances from a metabolic standpoint.

Digestion of Fat.—The gastric juice seems to have the power of digesting emulsified fats, such as occur in milk and egg-yolk. The main digestion, however, takes place in the small intestine. There is a large amount of active lipase in the pancreatic secretion and this is rendered more active by the presence of bile. Lipase is also secreted by the intestinal wall. The secretions poured into the duodenum are alkaline, and the fatty acids from the hydrolysis of the fats unite with the alkali to form soaps, which in turn aid the emulsification of the rest of the fat. The bile also aids in the solution of the fatty acids and soaps. When the fats have been broken down into soaps and fatty acids they, together with glycerol, are absorbed by the intestinal wall and there resynthesized into fats. In the form of a milky emulsion the greater part of the fat absorbed finds its way through the thoracic duct, but some passes directly into the blood stream. Since the digestion of fat is rather slow, the increased presence of fat in the blood becomes manifest several hours after the ingestion of a meal and persists from eight to fourteen hours after the food is taken. The fat is usually withdrawn from the blood

quite rapidly and oxidized or stored. Unless foreign fats have been given in large amounts, the material stored resembles not the fat ingested but the fat which is characteristic of the animal itself.

The absorption of fat depends upon the amount and the nature of the food ingested. Emulsified fats are almost completely absorbed. Fats with a low melting point, such as butter and olive oil, are absorbed better than mutton fat, which has a relatively high melting point. The amount of fat ingested has an important bearing on the amount absorbed. Rubner found that bacon and butter were well absorbed in amounts of 200 gm., but when 350 gm of fat were given in the form of butter and bacon there was a loss of 12.7 per cent. in the feces.

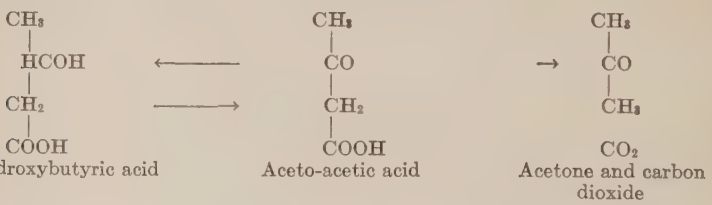
The oxidation of fats can be represented by taking tripalmitin, $C_{51}H_{98}O_6$ as an example:

$$\underset{806}{C_{51}H_{98}O_6} + \underset{2320}{72.5\ O_2} = \underset{2244}{51\ CO_2} + \underset{882}{49\ H_2O}$$

(molecular weights.)

The respiratory quotient is therefore $\frac{51}{72.5} = 0.703$ and the calorific value of a liter of oxygen 4.72 or, according to other calculations, 4.686. It will be noted that 806 gm. of tripalmitin, uniting with a large amount of oxygen, forms not only carbon dioxide but also 882 gm. of water. This means that fat really furnishes to the body more than its own weight in water when it is oxidized.

The Ketones.—It seems probable that the normal oxidation of fat forms at one stage *aceto-acetic acid* (diacetic acid). This through reduction may form beta-oxybutyric acid or it may form acetone by splitting off carbon dioxide.



Beta-hydroxybutyric acid — Aceto-acetic acid — Acetone and carbon dioxide

Aceto-acetic acid may also be derived from several of the amino-acids, such as leucine, tyrosine, and histidine. It was long known that these three ketone bodies made their appearance in the urine of diabetics and that the amount was roughly proportional to the diminution in the oxidation of carbohydrate. Rosenfeld as early as 1885 said that the fats burn in the fire of carbohydrate. In 1910 Woodyatt took up the question of antiketogenesis, the prevention of the formation of ketones, and suggested that the basis was a certain type of reaction in which one molecule of aceto-acetic acid would react with one molecule of an alcohol or glucose. Zeller found that when the percentage of calories furnished by carbohydrate was changed from 25 to 10 per cent., acetone appeared in the urine and increased as the carbohydrate ration was diminished. Lusk, commenting on this, suggested that the normal combustion of each mole-

cule of beta-oxybutyric acid required the presence of a triose molecule from carbohydrate. In 1921 Shaffer and also Woodyatt studied the question in greater detail and demonstrated independently that the fatty acid molecule was completely oxidized only when one molecule of glucose was oxidized at the same time in the same place. If less than one molecule of glucose is available aceto-acetic acid is not oxidized to carbon dioxide and water but is liberated in the blood together with its product, beta-oxybutyric acid. The smaller the proportions of glucose the larger are the amounts of the ketones.

It is a matter of great practical importance to be able to calculate the total fatty acids and the total glucose and their ratio in a diet or mixture of food which is being metabolized. The method used by Woodyatt is as follows:

$$\frac{\text{Fatty acids}}{\text{Glucose}} = \frac{\text{F A}}{\text{G}} = \frac{\text{0.44 Prot.} + \text{0.9 Fat}}{\text{Carb.} + \text{0.58 Prot.} - \text{0.1 Fat}}$$

The chief source of fatty acid is fat since these substances constitute about 90 per cent. of the molecule. Glycerol, which forms the other 10 per cent., is considered to be a source of glucose. One hundred gm. of protein contain certain amino-acids which furnish as much aceto-acetic acid as do 46 gm. of fatty acid and certain other amino-acids which furnish as much glucose as do 58 gm. of carbohydrate. Carbohydrate may be considered as furnishing 100 per cent. of its weight as glucose, though this relationship is not quite exact in the case of starch. Woodyatt finds the initial ratio for ketonuria is $\frac{\text{F A}}{\text{G}} = \frac{1.5}{1}$. In other words, ketosis appears if the total fatty acids metabolized are one and a half times as heavy as the total glucose metabolized. Shaffer used the method of calculating out the molecular weights of the fatty acid and glucose. This is more scientific but not quite as convenient for the practitioner. In some later work Shaffer has brought forward evidence to show that one molecule of glucose is sufficient to aid in the oxidation of two molecules of fatty acid. Under ordinary conditions, however, it is necessary for the body to oxidize one molecule of glucose for one of fatty acid in order to prevent ketosis since, on account of the wide area of the body, the glucose may not be oxidized in sufficient concentration in the cells where it is needed. Therefore, in clinical work we use the safer ratio and the threshold of ketosis. Shaffer has shown that this corresponds rather closely to the total respiratory quotient of 0.76. The triangle given on page 41 shows the relationship of this threshold (line *KA*) to the percentages of calories furnished by protein, fat, and carbohydrate. It will be noted that if protein furnishes only 10 per cent. of the calories, at least 16 per cent. must come from carbohydrate in order to prevent ketosis. If protein provides more than 44 per cent. of the calories, there will be no ketosis even in the total absence of carbohydrate metabolized as such. This is on account of the fact that protein furnishes more than enough glucose molecules to oxidize its fatty-acid molecules.

In diabetes mellitus the total excretion of ketones given in terms of beta-oxybutyric acid may be as great as 80 to 120 gm. a day. In normal

fasting subjects we rarely find more than 5 to 20 gm. The cause of the ketosis is probably identical in both cases. The condition is more severe in diabetes because in severe cases most, if not all, of the glucose derived from protein, is excreted in the urine. The normal fasting man can oxidize this glucose from protein. Patients with fevers and other severe diseases, when subsisting on diets which contain but little carbohydrate, may also have ketosis.

In calculating the threshold of ketosis we must always consider the material metabolized by the patient, not the material given in the diet. The amount of protein metabolized should be determined from the nitrogen of the urine, which is often very different from the amount in the food. The carbohydrate should be estimated in diabetes by the difference between that which is ingested and that which is excreted, or better still by actual determinations made by some respiration apparatus. The fat metabolized will be furnished in part by the food and in part by the body unless the calories of the diet are sufficient to cover the total requirement. A practical method of determining the total fat metabolized is as follows: Calculate the total calorific requirement by adding to the estimated basal an amount sufficient to cover the estimated muscular activity. Subtract from this the protein and carbohydrate actually metabolized. The remaining calories must be derived from food fat and body fat.

It sometimes happens, as in the case of the Newburgh and Marsh diet, that the fat in the food greatly exceeds the fat metabolized. Such an excess is stored and does not furnish fatty acids. This is demonstrated in the calorimeter studies of Richardson and Mason[1] and Richardson and Ladd.[2] They have shown that the appearance of ketosis depends on the fatty acid-glucose ratio of the mixture metabolized, which may be very different from the ratio given in the food.

THE PROTEINS

The proteins are the most important constituents of living cells. It seems probable that each plant or animal has its own specific form or forms. This means an almost infinite variety of proteins, which would seem incredible were it not for our knowledge of the chemical nature of these substances. Each protein is composed of a large series of *amino-acids*, which are usually spoken of as its "building stones." These, like letters, can be arranged in a million different ways, giving us as many proteins as there are words in the dictionaries of all the languages.

The proteins of plants are manufactured from amino-acids which are probably made from ammonia and carbohydrate. In the animal body the proteins are built up from the amino-acids absorbed from the intestine as a result of the digestion of plant proteins or the proteins of the animals. Some amino-acids, such as glycocoll, may be built in the animal body; others may be formed in the intestinal tract as a result of bacterial action. There are, however, several amino-acids essential to life that can be derived only from certain plants whose proteins contain these building stones or from the flesh or milk of animals which have eaten these plants.

[1] *Jour. Biol. Chem.*, 1923, **57**, 587.

[2] *Ibid.*, 1924, **58**, 931.

The proteins are the substances which contain the organic nitrogen of the body. The composition of a typical protein is as follows: C, 50 per cent.; H, 7 per cent.; N, 16 per cent.; O, 22 per cent.; P, 0.4 per cent.; S, 0.3 per cent. Their molecules are very large, too large to go through parchment, and the estimations of their molecular weights are in the neighborhood of 14,000 to 16,000. It is difficult to isolate pure proteins as they usually occur in combination, and it is also difficult to study them chemically on account of the ease with which they are altered by simple manipulations.

The following classification of proteins suggested by the American Society of Biochemists is given by Matthews.[1]

Classification of Proteins Proposed by the American Society of Biochemists.

I. **The Simple Proteins.**
   - A. Albumins.
   - B. Globulins.
   - C. Glutelins.
   - D. Prolamines.
   - E. Albuminoids.
   - F. Histones.
   - G. Protamines.

II. **Conjugated Proteins.**
   - A. Chromoproteins.[2]
   - B. Glyco- or glucoproteins.
   - C. Phosphoproteins.
   - D. Nucleoproteins.
   - E. Lecithoproteins.
   - F. Lipoproteins.[3]

III. **Derived Proteins.**
   - A. Primary Protein Derivatives.
     - (*a*) Proteans.
     - (*b*) Metaproteins.
     - (*c*) Coagulated proteins.
   - B. Secondary Protein Derivatives.
     - (*a*) Proteoses.
     - (*b*) Peptones.
     - (*c*) Peptides.

When proteins are eaten the stomach secretes hydrochloric acid and an enzyme, pepsin. These attack the outer layers of the bolus of food and start the digestion of the proteins, reducing them to the state of acid albumen and proteoses. Some polypeptides, tri- and dipeptides, may be

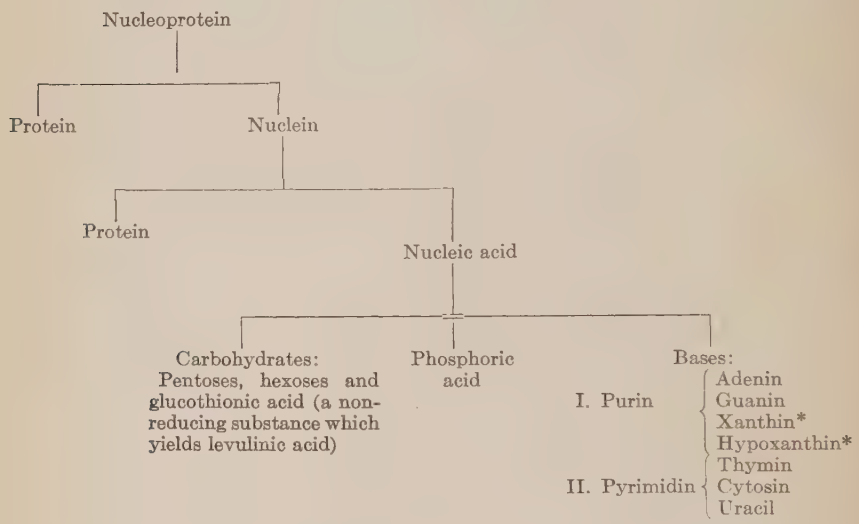
[1] *Physiological Chemistry*, New York, Wm. Wood & Co., 1921.

[2] The subdivision here called chromoproteins is called "hemoglobins" in the usual American classification. The word chromoprotein has so many points of superiority over that recommended by the Society that it has been adopted here. It was adopted by the English classification. (Matthews.)

[3] Artificial lipoproteins are easily made. This subdivision has been added by Matthews to the classification adopted by the Society.

formed. Some protein masses may pass unaltered into the intestine. Here the digestive process is continued by the pancreatic and intestinal juices, with their ferments, enterokinase, trypsin, and erepsin, breaking up the proteins by means of hydrolysis and liberating the amino-acids. The nucleoproteins are acted upon by special ferments and in their breaking down liberate amino-acids, phosphoric acid, and several other substances. The amino-acids are absorbed by the intestinal wall and then carried by the blood to the tissues where they serve to replace the wear and tear of tissue waste or else are manufactured into the specific protein characteristic of the animal species.

TABLE 6.



* Formed in a secondary reaction from adenin and guanin.

The table on page 55, taken from L. B. Mendel's recent lectures on nutrition show the amino-acids contained in some of the important proteins. The analysis of protein is difficult, and even our best figures are only approximations as to the actual percentage. It will be noted that some of the proteins lack glycocoll, lysine, and tryptophane, and the sulphur-containing amino-acid, cystine. These are essential to the growth of animals since the proteins characteristic of our experimental mammals cannot be formed without the building stones. This means that we must consider in our food not only the amount but also the source of the protein.

Gliadine from wheat is deficient in glycocoll; gelatine deficient in tryptophane; zein from maize deficient in glycocoll, tryptophane, and lysine. If young white rats are given a diet in which any one of these forms the sole source of protein the animals, after a few days, will cease to gain in weight and will not resume their normal rate of growth until the missing amino-acids are added to the ration.

TABLE 7.—QUANTITATIVE COMPARISON OF AMINO-ACIDS OBTAINED BY HYDROLYSIS FROM PROTEINS.*

Compiled for L. B. Mendel[1] by Dr. H. B. Vickery, 1923.

	Casein.	Gelatine.	Gliadine.	Zein.	Lactal-bumin.	Edestin.
Glycocoll	0.45	25.5	0.00	0.00	0.37	3.80
Alanine	1.85	8.7	2.00	9.79	2.41	3.60
Valine	7.93	0.0	3.34	1.88	3.30	6.20
Leucine	9.7	7.1	6.62	19.55	14.03	14.50
Proline	7.63	9.5	13.22	9.04	7.36	4.10
Oxyproline	0.23	14.1	?	?	?	?
Phenylalanine	3.88	1.4	2.35	6.55	1.25	3.09
Glutaminic acid	21.77	5.8	43.66	26.27	12.89	18.74
Oxyglutaminic acid	10.5	0.0	2.4	?	10.00	?
Aspartic acid	4.1	3.5	0.58	1.71	9.30	4.50
Serine	0.5	0.4	0.13	1.02	1.76	0.33
Tyrosine	4.5	0.01	1.61	3.55	1.95	2.13
Cystine		?	0.45	?	1.75	1.00
Histidine	2.5	0.9	1.49	0.82	2.61	2.19
Arginine	3.81	8.2	2.91	1.55	3.47	14.17
Lysine	7.62	5.9	0.63	0.00	9.87	1.65
Tryptophane	1.5	0.00	1.0	0.00	2.4	1.5
Ammonia	1.61	0.4	5.22	3.64	1.31	2.22
Total	90.17	91.31	87.61	85.27	83.41	83.78

* The analyses are combinations of what appear to be the best determinations by various chemists.

The growing organism obviously needs proteins with the proper amino-acids to construct new tissue. The need of the adult organism is not quite so clear. There is, of course, a constant breaking down of tissues as blood cells are destroyed, epithelial cells cast off the skin or into the intestinal tract, etc. This loss could probably be covered by a small amount of nitrogenous food. There seems to be an additional constant breaking down of all body tissues, with a constant replacement from the blood. In this destruction of body protein the amino-acids are probably liberated just as in digestion and doubtless are used in part for the reconstruction of body tissue in other places. Not all of the material, however, seems to be available and there is a constant small loss to the body. We are reminded of the loss of specie which occurs in any country. A certain issue of money is minted in the treasury and goes into circulation. It is stored in banks, withdrawn again into circulation, stored again in banks, etc. If the issue be counted each year it will be found that there is a steady small loss due to the disappearance of coins through various accidents. This loss must be replaced by the minting of more bullion, just as the body replaces its tissue by the utilization of more protein. The loss of specie is not necessarily augmented when the transfers of each are increased by the normal methods of exchange. It does, however, become much greater than normal during periods of national or local disorder. In a similar fashion the breaking down of body protein does not increase with normal muscular activity, but rises with leaps and bounds during such general calamities as severe infections or malignant growths.

[1] *Nutrition,* Yale University Press, New Haven, 1923.

The average adult American or European consumes daily about 60 to 120 gm. of protein. Of this he needs only 14 to 25 gm. a day for the replacement of body tissue. This is called by Rubner the "Wear and Tear Quota." The remainder of the protein ingested is used as fuel, perhaps some of it is utilized in a more active replacement of body tissue, but there is no evidence that such a replacement above the wear and tear minimum is of any value to the organism. We can demonstrate the wear and tear quota of normal or sick persons by giving a diet which contains enough calories to supply the body needs, taking care that a sufficient proportion of these calories are in the form of carbohydrates. The diet should contain either practically no protein at all or an amount smaller than the wear and tear quota, given in divided doses throughout the day. When such a diet is started the body will slowly get rid of the small amount of nitrogenous material loosely stored in the blood and tissues. This was called "circulating protein" by Voit, "surplus cellular nitrogen" by Benedict, and "deposite protein" by Lusk.[1] When, after three or four days, this has been largely eliminated, the nitrogen of the urine will represent fairly accurately the protein metabolism. Protein contains 16 per cent. of nitrogen, which is eliminated by the kidneys in the form of urea, etc., when the molecule is broken down in the tissues. Therefore, each gram of urinary nitrogen means that 6.25 gm. of protein have been metabolized. Under the conditions above described a normal man on the fourth day of the low-protein, high-carbohydrate diet will excrete 2.2 to 4 gm. of nitrogen, which means that 13.75 to 25 gm. of protein have been metabolized. This is called the *nitrogen minimum*.

On such a diet the body will be in negative nitrogen-balance unless the food contains just enough of a good quality protein to cover the wear and tear quota. Thomas[2] has shown that this can be administered in divided doses in such a manner that the total protein metabolism is not increased, the new material passing into the cells at just the same rate as it leaves them. He has maintained nitrogen-balance in himself on a ration containing only 30 gm. of meat protein. This can be done in the case of meat or milk protein, since these contain about the same amino-acids which are used in the construction of human protein. Other proteins, notably those from plants, do not contain enough of the necessary building stones and therefore larger amounts must be consumed to obtain the requisite amount of all the materials needed. This is illustrated by the following table quoted from Thomas by Lusk.[3]

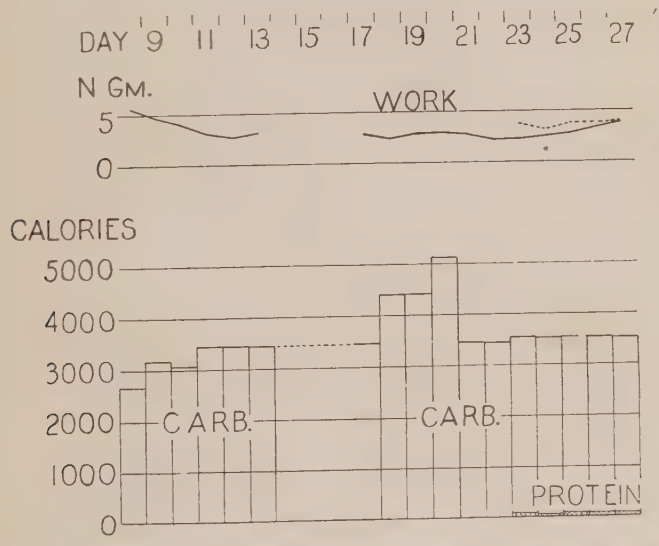
TABLE 8. — AMOUNTS OF VARIOUS PROTEINS REQUIRED TO PROTECT THE BODY PROTEIN FROM LOSS.

	Grams.
Meat protein	30
Milk protein	31
Rice protein	34
Potato protein	38
Bean protein	54
Bread protein	76
Maize protein	102

[1] *Elements of the Science of Nutrition*, 3d ed., W. B. Saunders Co., Philadelphia, 1917.
[2] *Arch. f. Physiol.*, Suppl., 1910, p. 249.
[3] *The Fundamental Basis of Nutrition*, Yale University Press, New Haven, 1923.

One very practical application of this is found in all diets in which we are anxious to reduce the protein metabolism to a minimum. This is particularly important in nephritis and diabetes. Some clinicians give a protein-free diet, but this, of course, does not reduce the protein metabolism below the wear and tear quota. We reduce the protein metabolism best by giving a high-calory diet, preferably one rich in carbohydrates if these can be utilized. The diet may contain 30 gm. of meat or milk protein in divided doses without increasing the protein metabolism in the slightest, since this merely replaces the body protein. The proteins of bread or maize in similar amounts would not replace body protein nearly as effectively.

FIG. 7.



Experiment of Karl Thomas on his nitrogen minimum. He found that his nitrogen excretion was 7.5 gm. a day during starvation and about the same when he took a pure fat diet. He then shifted to a pure carbohydrate diet as shown in the chart. The nitrogen in the urine fell to 2.2 to 3 gm. a day and was not increased by heavy muscular exercise on three successive days or by the ingestion of 2 to 3 gm. of nitrogen in the form of animal protein in small divided doses.

We have spoken of the value of a diet rich in carbohydrates in diminishing the protein metabolism. This has been demonstrated by Karl Thomas in a series of heroic experiments on his own body while performing his daily work in the laboratory. The chart made from his data shows that the nitrogen excretion obtained during starvation was 7.5 gm. This was about the same as the figure when a pure fat diet was ingested. Apparently, the food fat merely took the place of body fat. When an ample diet of carbohydrate was consumed we note the rapid fall in nitrogen elimination as the body rid itself of the "deposit protein," and finally the establishment of the "nitrogen minimum" between 2.2 and 4 gm. This was not increased by the addition of a corresponding amount of protein in small divided doses.

This brings us to the question of the *optional protein ration*, a question that will never be settled. Dietary studies show that in this country many hard working men and athletes consume 100 to 200 gm. of protein daily. We have seen that nitrogen-balance may be maintained on 30 to 40 gm. daily. Somewhere in between 30 and 200 gm. lies the broad zone of the optimum. We cannot use diets as low as 30 to 40 gm. except in short experiments because they must be adjusted with extreme care as to the character of the protein and its method of administration. The diet is unnatural in that it lacks flavor and requires a distasteful proportion of carbohydrate. Man is by Nature carnivorous and he enjoys the flavor of animal food. Even the vegetarians try to make foods which will resemble meat as closely as possible. We cannot introduce much flavor or satisfaction into a diet until we have added about 50 to 60 gm. of protein. Chittenden,[1] in his famous experiment on a group of soldiers, athletes, and professional men, used about this amount of protein, together with a somewhat low total caloric intake. The subjects remained in good health, maintained their body weight and strength. Hindhede advocated about this same level of protein metabolism but it is doubtful if the ordinary individual would be happy on such a ration.

Chittenden and Mendel, in the first edition of this work, give the following table showing the actual amounts of food eaten by various groups of individuals. It will be noted that the protein consumed by the football teams and the Maine lumbermen seems excessive. The proportion of protein to the total food is, however, not very great, since it furnished 14.2 per cent. of the calories for the athletes and only 10.5 per cent. for the woodsmen. They were eating such large amounts of food that the great excess of protein was probably taken as a necessary constituent of the bread, beans, etc., since almost all of the common foods, except sugar and butter, contain considerable amounts of nitrogen. The 66 gm. consumed by the Javanese seem small, but the total caloric intake was so low that the protein actually furnished 18.7 per cent. of the calories.

The football players and lumbermen were much larger than the Javanese and for this reason probably had a greater wear and tear quota. We cannot, however, be certain as to the relationship of nitrogen minimum to the size of the individual as this question apparently has not yet been studied. We naturally suppose that the wear and tear quota is proportional to the protoplasmic mass which in turn is proportional to the surface area. Fat probably acts as inert ballast, and it is somewhat illogical to give a certain amount of protein per kilogram of body weight. We have seen in the case of athletes and lumbermen that it is illogical to administer the protein calories as a certain percentage of the total, since the calories used for muscular work do not carry any extra demand for protein. As a matter of fact, protein used for fuel purposes is not as economical for muscular activity as carbohydrate.

[1] *Physiological Economy in Nutrition*, 1904.

SUMMARIZED RESULTS OF DIETARY STUDIES IN THE UNITED STATES (QUANTITIES PER MAN PER DAY.)

	Number of studies included in averages.	Actually Eaten.			Digestible.			Fuel Value.
		Protein.	Fat.	Carbohydrates	Protein.	Fat.	Carbohydrates.	
		Grams.	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Grams.*	*Calories.*
PERSONS WITH ACTIVE WORK.								
Rowing clubs in New England	7	155	177	440	143	168	427	3955
Bicyclists in New York	3	186	186	651	171	177	631	5005
Football teams in Connecticut and California	2	226	354	634	208	336	615	6590
PERSONS WITH ORDINARY WORK.								
Farmers' families	10	97	130	467	89	124	453	3415
Mechanics' families	14	103	150	402	95	143	390	3355
Laborers' families in large cities	12	101	116	344	93	110	334	2810
Laborers' families in more comfortable circumstances	2	120	147	534	110	140	518	3925
PROFESSIONAL MEN.								
Lawyers, teachers, etc	14	104	125	423	96	119	410	3220
College clubs	15	107	148	459	98	141	445	3580
MEN WITH LITTLE OR NO EXERCISE.								
Men in respiration calorimeter	11	112	80	305	103	76	296	2380
PERSONS IN DESTITUTE CIRCUMSTANCES.								
Poor families in New York City	11	93	95	407	86	90	395	2845
Laborers' families in Pittsburg, Pa	2	80	95	308	74	90	299	2400
MISCELLANEOUS.								
Negro families in Alabama	20	62	132	436	57	125	423	3165
Negro families in Virginia	19	109	159	444	100	151	342	3625
Italian families in Chicago	4	103	111	391	95	105	379	2965
French Canadians in Chicago	5	118	158	345	109	150	335	3260
Bohemian families in Chicago	8	115	101	360	106	96	349	2800
Inhabitants of Java Village, Columbian Exposition, 1893	1	66	19	254	61	18	246	1450
Russian Jews in Chicago	10	137	103	418	126	98	405	3135
Mexican families in New Mexico	4	94	71	613	86	67	595	3460
Chinese dentists in California	1	115	113	289	106	107	281	2620
Chinese laundrymen in California	1	135	76	566	124	72	549	3480
Chinese farm laborers in California	1	144	95	640	132	90	621	3980
Fruitarians	6	50	102	237	43	92	225	2055
Maine lumbermen	.....	182	337	812	.....	.....	.....	6995

How then should we plan the protein ration? It is foolish to pretend that we can adjust the intake so as to correspond exactly with the optimum. There are too many uncertain factors. Four main points have to be considered: (1) The size of the individual, (2) the need for extra protein in the growing or convalescent organism, (3) the quality of protein, and (4) the preference of the physician for a high- or low-protein diet. The practice of the metabolism ward of the Russell Sage Institute of Pathology has been as follows: The physician "sizes up" the patient and decides without any elaborate calculation how many grams of nitrogen he wants to give in the food. The nurses see that enough of the protein is given in the form of meat, eggs, and milk to cover the wear and tear quota. Of course, the amount of protein ordered depends on the character of the diet used for experimental or therapeutic purposes. Ordinarily the quantity employed is about 62 to 75 grams (10 to 12 gm. of nitrogen).

The personal preference of the physician or dietitian will depend upon his beliefs regarding the relative advantages of a high- or low-protein diet. The advocates of the *low-protein* ration state with justice that protein foods are expensive and that a surplus of protein is almost useless to the organism and, moreover, causes an unnecessary amount of work on the part of the kidneys. They make several other claims which do not seem to be as yet fully substantiated by experimental proof. They state that the low-protein diet diminishes intestinal putrefaction and therefore decreases the absorption of toxic products which harm the organism. They claim that a low-protein diet leads to greater strength and endurance and a freedom from minor ailments. Some believe that a low-protein diet tends to prevent the development of nephritis, diabetes, and several other diseases, ranging all the way from eczema to cancer.

The advocates of a *liberal protein* ration point to the danger of approaching too closely to the minimum compatible with health. They believe that one should steer wide of this danger by giving an ample surplus. They point to certain experiments in which animals have done badly on low-protein rations, though our newer knowledge of vitamines and the importance of certain amino-acids may change the significance of these experiments. They use as an argument the fact that most men select a rather high-protein ration if they can afford it and that, on the whole, the classes which consume 120 to 180 gm. of protein a day are stronger and less susceptible to disease than those who take less than 100 gm. This argument is weakened by the fact that those who take less than 100 gm. daily are the poorer classes subsisting under bad hygienic conditions.

It seems to me that the one great argument for a diet which contains over 75 gm. of protein is that it tastes better. For this reason it may be possible to substitute protein for fat and carbohydrate, which tend to produce obesity with its very real dangers. The great disadvantages of a high-protein ration is the extra work thrown on the kidneys. If these organs are functionally below the normal they may suffer as a result of the increased strain. The medical profession as a whole believes that people in comfortable circumstances eat too much and that their meat

consumption is excessive. This general impression regarding too much meat must be heeded even though it is not yet supported by statistical proof.

In long experiments the protein metabolized by the body will equal the protein absorbed from the food provided that enough calories are given to cover the expenditure and enough protein to cover the wear and tear quota. Thus, nitrogen-balance may be established at a level of 3 gm. or 12 gm. or 40 gm., etc. If the calories of the food are not sufficient, some of the body fat and protein will be sacrificed and the individual will show a negative nitrogen-balance. If the food is ample and the subject is growing or is recovering from an illness, there may be a storage of protein and a positive nitrogen-balance. In either of these cases we should judge the protein metabolism not from the nitrogen of the food but rather from the nitrogen of the urine. This sounds obvious, but it is a fact often forgotten by clinicians.

Protein Metabolism in Disease.—In the milder forms of disease the protein metabolism seems to be practically normal. If there are not toxins circulating in the body there does not seem to be any increase in the protein destruction. Thus, we may find a nitrogen minimum in arthritis deformans and in the chronic stages of syphilis which does not exceed that of normal controls. In certain stages of malignant disease, however, and especially in the toxic stages of fever, it is impossible to reduce the wear and tear quota to the level of 2 or 3 gm. found in health. Shaffer and Coleman,[1] Hocker,[2] and others gave typhoid patients diets which contained more than enough calories to cover the requirement but only allowed 2 to 4 gm. of nitrogen a day. The nitrogen of the urine remained between 7 and 15 gm. a day. Their nitrogen-balance was therefore strongly negative, remaining so until they gave 8 to 18 gm. of nitrogen in the food and about twice as many calories as the patient actually produced. This indicates a distinctly abnormal factor, which is usually spoken of as the "toxic destruction of protein." It is believed that the poisons break down the protein tissues at a rate much faster than normal. The category of diseases has not yet been thoroughly explored. There does not seem to be much change in the protein metabolism in exophthalmic goitre and McCann and Barr[3] have shown that the nitrogen minimum in tuberculosis does not greatly exceed the normal limits. Other fevers, such as erysipelas, with greater toxemia, seem to resemble typhoid. It is perhaps impossible to estimate the true protein metabolism in nephritis or cardiac failure with œdema because in these conditions the nitrogen excretion furnishes no true guide as to the amount of nitrogen metabolized daily by the tissues.

In starvation and in the temporary or chronic state of undernutrition which is so common, the protein metabolism is increased because the body protein is used as a fuel to supply the caloric requirements. Such an increased protein destruction can be greatly diminished by the administration of carbohydrates, since these spare the protein much more than

[1] *Arch. Int. Med.*, 1909, **4**, 538.
[2] *Deutsch. Arch. f. klin. Med.*, 1914, **115**, 82.
[3] *Arch. Int. Med.*, 1920, **26**, 663.

fat given in the food or fat withdrawn from the storehouses within the body. It is therefore not surprising that we sometimes find an exceedingly high nitrogen elimination in certain cases of severe diabetes. Thus, the classical patient, C. K., studied in the Sage calorimeter[1] excreted from 35 to 38 gm. of nitrogen a day for a short period. Joslin's[2] patient, No. 1011, excreted 13.5 gm. of nitrogen although the body weight was only 27.2 kilograms. She must have received about 40 per cent. of the total heat from the metabolism of protein, a percentage which is found in normal men only after they have taken an exceedingly large protein meal. In typhoid fever we not infrequently find 25 to 30 gm. of nitrogen in the urine, representing the destruction of 156 to 187 gm. of protein daily, almost all of this being derived from the body tissues. In pneumonia the protein metabolism is also increased but is somewhat masked by the accumulation of nitrogenous products in the consolidated lung. This may be released suddenly after the crisis and Svenson reported a patient who eliminated 40.8 gm. of nitrogen on the day after the temperature returned to normal.

The Products of Protein Metabolism.—In the growing organism a portion of the protein which has been broken down into amino-acids is resynthesized into body protein and deposited without affecting the metabolism. In the adult organism a small amount is deposited in similar fashion to replace the wear and tear quota, which represents the protein katabolized in the tissues. The excess of protein above this quota is burned as fuel. Approximately 58 per cent. of the protein molecule forms glucose, and this is apparently utilized in exactly the same fashion as glucose derived from ingested carbohydrate. The remaining portion of the protein which contains the nitrogen is incompletely oxidized, and the nitrogen is excreted by the kidney almost entirely in the form of urea. *Urea*, $CO(NH_2)_2$, is the diamide of carbonic acid, and it still contains potential energy, furnishing 2.52 calories per gram when burned in a bomb calorimeter. It cannot be oxidized in the body. A certain amount of water is required for the solution of urea so that it can be eliminated by the kidney, and this constitutes one of the fixed needs of the body. A man taking a large amount of protein or urea in his diet must be provided with sufficient water or else the kidney cannot perform its function.

The deamination of protein is also a source of ammonia. Our previous views regarding the site of formation of this substance have recently been changed by S. R. Benedict, who has shown that it is formed by the kidney but not in the liver or other tissues of the body.

Creatine and Creatinine.—The urine contains various other nitrogen-containing substances beside urea and ammonia. Among these are creatine, methyl-guanidine acetic acid ($C_4H_9N_3O_2$) and its anhydride creatinine ($C_4H_7N_3O$). The source of these substances is not clear, but the important fact remains that man excretes an extraordinarily constant amount of creatinine each day, usually between 0.8 and 2 gm. The amount for a given individual varies but little, being almost inde-

[1] Gephart, F. C., Aub, J. C., Du Bois, E. F., and Lusk, G.: *Arch. Int. Med.*, 1917, **19**, 908.

[2] *Treatment of Diabetes Mellitus*, 3d ed., Lea & Febiger, Philadelphia and New York, 1923.

pendent of the protein intake. Large men excrete more than small ones, suggesting a relationship to the body weight or perhaps more closely to the protoplasmic mass or the surface area. Creatine is excreted in much smaller amounts which depend to a certain extent on the amount of creatine ingested in the form of meat, beef extract, etc. Children and women seem to respond more to the ingestion of creatine than men.

Fasting tends to decrease the excretion of creatinine, but it increases the creatine. A similar increase is found in other conditions when the carbohydrate of the food is deficient and the creatine elimination may be high in wasting fevers with insufficient diet and a consequent breaking down of much body tissue. There is also a rise in creatine excretion in women during menstruation, pregnancy, and especially just after childbirth. Creatinine is probably derived from creatine, which is either ingested in meat or else derived from the body's own protoplasm. This is evidently not the sole source, since infants on a milk diet and vegetarians on a creatine-free diet excrete creatinine.

The Purines.—The purines are of great interest, especially the most important in human metabolism, *uric acid*. We have shown in the diagram that, from the breaking down of nuclein, we may obtain adenin and guanin, which may in turn form xanthin and hypoxanthin. These, by the action of enzymes in the tissues and especially in the liver, may be oxidized to uric acid. In some animals the uric acid is oxidized to allantoin, but this probably does not occur in man, and the human urine contains but small traces of this latter substance. Uric acid given subcutaneously to man is quantitatively excreted, and an increase in the purines in the diet is followed by an increased output, but the extra amount excreted is only a small fraction of the extra amount ingested. The fate of the remainder is not clear.

The nucleoproteins are not the sole source of uric acid, and birds are able to transform urea to uric acid, excreting most of the nitrogen in this form. The human organism evidently has the power of forming uric acid from some endogenous source. If a man is given a purine-free diet of milk, eggs, fats, sugars, bread, and potatoes, there is a daily, constant excretion of 0.3 to 0.5 gm. of uric acid.

Hippuric Acid.—Hippuric acid, benzoyl-glycin, $C_9H_9NO_3$, is found in large amounts in the urine of horses and cows. In man the excretion is usually small, but 1 or 2 gm. a day may be eliminated if the diet contains vegetables or fruits which yield benzoic acid. Cranberries are particularly rich in this substance. The body neutralizes the toxic benzoic acid by pairing it with glycocoll, an amino-acid. In man this is probably derived from the proteins of the food, but in the herbivora it is probably formed by synthesis. Amino-acids in small amounts are also found in the human urine. Phenol, ethereal sulphates, indican (indoxyl-sulphuric acid), and scatole (scatoxyl-sulphuric acid) are of importance as indicators of intestinal putrefaction.

Folin[1] in 1905 made an exceedingly important contribution to our knowledge of the composition of the urine by analyzing completely the daily excretion of a number of individuals on an ample purine-free diet.

[1] *Am. Jour. Physiol.*, 1905, **13**, 117.

He calculated the percentage distribution of the nitrogen among the various constituents *under one set of experimental conditions.* This method of complete analysis and calculation of the percentage distribution, the so-called *nitrogen partition,* once had a great vogue among clinicians in this country. There is a fundamental error in paying much attention to the mere percentage distribution. The urea nitrogen which forms the great bulk of the total depends upon the protein metabolism, and it may vary from 2 to 30 or more grams, depending on the level of the protein metabolism. The creatine nitrogen is constant and independent of the protein. On a low-protein diet it will form a large percentage of the total; with a high-protein metabolism due to disease it will constitute a small percentage. The *ammonia nitrogen*, which has received most attention, is of considerable value if we consider its total amount rather than the percentage figure. Ammonia is one of the agents with which the body neutralizes acids, but it is not the sole agent. The body utilizes the requisite amount of ammonia without any particular regard to the total nitrogen eliminated. The body has no budget system arranged on a percentage basis. The clinician who receives a report of the complete analysis of a day's urine should take into account the diet, the patient's own metabolism, and the total amount of each constituent. There is no formula which will take the place of a knowledge of the human metabolism, and laboratory methods are brought into discredit if interpreted blindly. In the case of the nitrogen partition there were the fundamental errors cited above, but it is quite probable that most of the serious errors were due to the ammoniacal fermentation of urea in the bladder or in dirty urinals. The utmost precaution must be taken to prevent such a formation of ammonia outside the body.

Metabolism of Alcohol.—When alcohol is ingested it is absorbed rather rapidly and 98 per cent. or more is oxidized by the body tissues, only a a small amount escaping through the breath and urine. The metabolism can be followed in respiration experiments because the respiratory quotient is very low, 0.666. The caloric value of alcohol is rather high, 7.07 calories from each gram. It may, therefore, be used to a limited extent as a substitute for carbohydrate or fat and, since it is not converted into sugar in diabetes may be of some theoretical advantage in this condition, though its antiketogenic value is very doubtful. It is rather difficult to conceive of any possible advantage over carbohydrate in other conditions. Alcohol may be considered a food because it is oxidized by the body, but the same might be said of morphine or caffeine. Alcohol should more properly be classed as a flavoring substance or as a drug, since the toxic effects outweigh the fuel value. The long-winded discussion as to whether or not alcohol is properly called a food has nothing to do with the prohibition question, although it has long befuddled the partisans of both sides.

Alcoholic beverages have been used in the treatment of certain diseases, especially fevers. They are easily taken by those who are accustomed to their use. At present it is safe to say that the majority of clinicians have stopped giving alcohol, since they believe that the toxic effects are harmful and that it is much better to give ordinary foods. Some still

employ liquors or wines as a flavoring to tempt capricious appetites. In this country a few advocate the use of malt liquors or wines in convalescents or in patients who need to be fattened. In Europe the moderate use of wine and beer is so customary that they usually form a part of the diet ordered by the physician. The question of prohibition is already complicated and the medical profession should not allow the public to place undue emphasis upon the value of alcohol in therapeutics since this is relatively unimportant. Physicians must compare the doubtful benefit of alcohol with the manifest injury caused to thousands of patients and their families.

The Blood.—It is beyond the scope of this article to discuss fully the many constituents of the blood. An excellent table giving the figures for normal and pathological blood has been published by Victor C. Myers.[1]

The blood serves to transport various substances from one part of the body to another and its composition changes after meals as food is being absorbed from the intestine. For this reason it is important to observe the standard conditions with regard to time of day, etc. We have spoken of the various factors which affect the blood sugar. Similar factors, though perhaps not so numerous, may affect all the other constituents, and the clinician should not interpret the results of any one determination without carefully considering the condition of the patient at the time the blood was drawn. The cautious practitioner will also remember the limitations of laboratory technique and the laboratory technician. Particular attention should be given to the length of time which has elapsed before the blood is analyzed. If the blood gases are being studied precautions should be taken to prevent diffusion into the atmosphere. Finally, we should remember that the picture given by one analysis is merely an instantaneous snapshot, Repeated analyses are of much more value. Often a functional test alone will furnish the information needed.

The Water Balance.[2]—Practitioners often try to estimate the water balance of a patient, and it is surprising to note the general ignorance of the principles which underly such a test. They all recognize the obvious sources of water in the fluids swallowed as fluids. They usually neglect very large amounts of water contained in the so-called solid foods. For example, a potato is 75 per cent. water; a tomato 94 per cent. Junket contains exactly as much water as milk; a hard-boiled egg just as much as a raw egg, yet the two solids would not ordinarily be classed as sources of water. Under certain conditions the water contained in the so-called solid foods exceeds in amount the total bulk of the so-called fluids. There is a third source of water which is usually entirely neglected, namely the water which, with carbon dioxide, is formed by the oxidation of carbohydrate, fat, and protein.

TABLE 9.

100 grams starch furnish	55.5 gram water
100 gram protein furnish	41.3 " "
100 grams fat furnish	107.1 " "
100 grams alcohol furnish	117.4 " "

[1] Barker's *Endocrinology and Metabolism*, D. Appleton & Co., New York, 1922, **3**, 424.

[2] Consult Soderstrom, G. F., and Du Bois, E. F.: *Arch. Int. Med.*, 1917, **19**, 931; Rowntree, L. G.: *Physiol. Rev.*, 1922, **2**, 116.

This table shows that fat furnishes more than its own bulk of water because it contains a large amount of hydrogen and unites with a large amount of oxygen from the air.

The exact determination of *water intake* of the patient is a matter of extreme difficulty. It requires the careful estimation of the water content of each raw foodstuff and an estimation of the loss or gain in cooking. In addition there must be an estimation of the water derived from the carbohydrate, fat, and protein actually metabolized, and if there has been any loss of body tissue we must take into account the water liberated from this source, since all the body tissues, even fat, are mixed with water. We must also take into account any loss of carbohydrate or salt, since both of these substances tend to hold water within the body, setting free the water when they are oxidized or excreted.

For ordinary purposes we can estimate the water intake by weighing the total food and drink administered to the patient. This is fairly accurate because the foods consist either of water or of protein, fat, or carbohydrate which form water. If we desire greater accuracy we might subtract from the total weight a small amount for cellulose and inorganic salts and about one-half the weight of the protein and carbohydrate.

The clinician usually estimates the *water output* by recording the volume of the urine. He often neglects the water contained in the feces, which may be considerable when patients have diarrhœa. If enemas are used it is necessary to measure the amount given and the amount recovered, and it is often surprising to find that a large amount of water is retained by the patient. The chief error is estimating the total output consists in neglecting the water vaporized from skin and lungs. This varies greatly with atmospheric conditions, but a large series of experiments on patients in the Russell Sage calorimeter with a temperature of 23° C. and a humidity of about 60 per cent. give an average of 700 gm. a day. The amount depends upon the total heat eliminated and patients with high metabolism or with a falling temperature vaporize much more water than normal men. Vaporization is increased when the air is very dry or when there is a draft. When the air is hot or humid sweating may appear, causing a great increase in the water given off from the skin. It is quite evident that the water vaporized from the physiological surface of the body may equal or exceed the water excreted by the kidneys. It is easy to realize this if we compare the large amount of water that we drink on a hot summer day with the small amount of highly colored urine that is eliminated.

It is impossible to estimate accurately the total water output unless we keep the patient all day in a respiration chamber. We can form an approximate idea of the total loss by adding to the total weight of water and feces about 700 gm. for the water vaporized under ordinary conditions.

For clinical purposes the best method of estimating the total gain or loss of water is by weighing the patient at the same hour each day. Fluctuations in weight are almost entirely due to changes in water content if the patient is receiving the proper amount of food. If there is any great loss or gain of body nitrogen we can estimate this roughly by allowing 100 gm. of muscle for every 3 gm. of nitrogen. Surplus calories will

usually be stored as fat, and we can allow about 1 kilogram of fat for every 900 calories. It is very much easier to weigh the patient than to measure the food. In the case of bed patients it is possible to construct a table which rests on the platform of the scales.

We must remember, however, that the old clinical procedure of charting the fluid intake and urine output serves the very practical purpose of reminding the nurse to give enough water in the case of fever patients, or a restricted amount of water in those who are œdematous. We should not neglect any possible means of impressing upon the nurses the importance of water in the diet. Water is by all means the most vital constituent of the dietary, though this is seldom realized by the attendants of the sick. Fever patients get very little water in solid foods and they eliminate an unusually large amount through the skin. They are often too sick to ask for water vigorously enough to secure the services of the busy nurses. They are often too sick to care whether or not they drink, and even if they do care to drink they may be too weak to do so unaided. In hospital wards which are understaffed the physician should eliminate all unnecessary therapeutic procedures until he is sure that the patients are receiving enough water. He should see that the urine is never allowed to become concentrated. He should insist that the patients get water at regular intervals. He should watch the patients' tongues and skins and should congratulate the nurse if there are evidences of a plentiful supply of water within the tissues. Indifference on the part of the nurses can easily be overcome by enthusiasm on the part of the doctor.

The importance of water is due to the fact that man is still living in a liquid medium. His cells are bathed in a fluid which probably resembles rather closely the primordial seawater from which we emerged when the world was young. The chemical changes of the body all take place in a watery solution, and the cells are highly susceptible to a concentration of this fluid. Dehydration of the body naturally involves a diminished blood volume, a concentrated blood, and a tendency toward concentrated tissue juices. If there is not enough water available the urea cannot be excreted through the kidney in normal amounts and it is in just such conditions as fever that the urea formation is greatest, owing to the toxic destruction of protein. The best example of the diastrous effects of dehydration is found in cholera. Here the excessive losses through the bowel are often accompanied by severe damage to the kidney. The condition is relieved by the proper administration of water under the skin or into a vein.

In certain diseases, such as nephritis or cardiac failure, there may be a visible œdema. In some cases it is presumably due to a retention of sodium chloride. This salt tends to retain water within the body on account of its osmotic pressure, and if the kidney is unable to eliminate salt in adequate amounts, water may be retained in the body. Although we are often disappointed by the results of a salt-poor diet, it is worth trying in most cases of œdema. Water may also be retained in rather surprising amounts in the form of an invisible œdema. It may also be retained in diabetic patients who are fasting, and it is startling to note a gain in weight in the man who is taking no food. A retention of water

may also occur in obese patients on low diets who are actually losing fat. Fatty tissue may be replaced by water, and the temporary failure of such a patient to lose weight should not be allowed to discourage those who conscientiously restrict their diets.

Water Drinking at Meals.—There has been a long-standing prejudice against drinking water with meals, although this has never been supported by experimental evidence. Hawk studied the question in a long series of careful observations made on normal men. He found that saliva acts most vigorously when diluted with about six volumes of water. He proved quite conclusively that the human stomach secretes large amounts of gastric juice when stimulated by distilled water; in fact, the secretion was about the same as after taking bouillon or coffee. Digestion in the stomach was increased rather than diminished when water was taken with meals, and the excess of fluid seemed to pass rapidly into the intestine. The pancreatic secretion was apparently increased and there were better utilization and absorption of fats and carbohydrates and proteins. There was also evidence of a diminished intestinal putrefaction. Hawk found no deleterious effects from distilled water and proved that twenty minutes after drinking a glass of very cold water (10° C.) the temperature of the stomach contents had returned to normal. He concluded that the drinking of a reasonable volume of water with meals is beneficial in normal individuals. He is rather careful not to make any sweeping statements with regard to patients with gastric disease, but he points out that in such maladies there is no evidence which indicates that water taken with meals is harmful.

THE MINERAL METABOLISM

There is an enormous literature dealing with the mineral metabolism, but it is characterized by conflicting results, discordant theories, and a general lack of certainty. This is largely due to the fact that the mineral constituents are present in small amounts and are by no means constant in plants or most animal tissues. Their excretion in animals is also variable, depending on many factors. Short experiments, therefore, are of little or no value. Our knowledge of these factors is still in its infancy, a point which has been recently proved by the newer work on rickets showing the importance of sunlight.

In the case of protein, fat, or carbohydrate we can study the actual combustion by means of respiration experiments. With the mineral constituents there is no similar method of following their utilization by the body, and we must content ourselves with a study of intake, output, and distribution in the fluids and tissues. The food ordinarily selected by man seems to contain an abundance of all the necessary minerals, and we can point to only a few diseases, such as goitre, certain anemias, and some bone diseases of infancy or pregnancy, in which a deficiency of salts is a definite etiological factor. There are several other diseases, such as tetany, rickets, and nephritis, in which the disordered mineral metabolism is due to some factor within the body. Still other manifestations may be produced experimentally by drastic overdosage or underfeeding of certain salts. There is still a vast unexplored territory and we may hope

that the minerals will be found to have a direct connection with many important diseases. It is not possible here to give more than a brief sketch of the important facts.

Calcium.—Calcium is one of the important mineral constituents, especially in growing children. According to Sherman, adults taking on an average 44 gm. of protein a day require about 0.45 gm. of calcium a day or 1 gm. of calcium for every 100 gm. of protein. Children between the ages of three and fourteen seem to require about 1 gm. of calcium daily. There is an increased demand for calcium during pregnancy and lactation in women and particularly in cattle. Milk is one of the best sources of calcium, and most dietitians advocate the use of a quart a day by the growing child. This calcium must be derived from the human mother or the cow. The calcium of vegetables can be utilized well by adults but not very well by children.

Phosphorus.—Phosphorus is perhaps more intimately connected with the life processes than any other mineral constituent. It is an important component of nervous tissue and protein, and plays a role in the intermediary metabolism of carbohydrate. Sherman has found that the adult requires daily about 0.88 gm. As we have said, our knowledge of phosphorus and calcium metabolism is being revised by the students of the rickets problem.

Iron.—Iron is, of course, needed for the hemoglobin of the blood. Sherman believes that the daily intake ought to be at least 12 mg. of food iron and considerably more than this during pregnancy and lactation. There has been a large amount of discussion as to whether or not iron in the form of inorganic salts is as well absorbed as the organic salts. There is evidence on both sides. Carter, Howe, and Mason[1] in their textbook on *Nutrition and Clinical Dietetics*, state: "Although inorganic iron appears to be as effective as organic iron it has been recommended by some that at least a part of the iron ingested be in 'organic' form."

Whipple found in dogs that sudden losses of blood due to hemorrhage are most rapidly replaced on diets of beef, liver, and hemoglobin. Clinical experience has shown the favorable action of Blaud's pills on some chronic anemias.

Chlorine.—The sodium chloride consumed by the average person amounts to 8 to 10 gm. daily, and perhaps double this amount is taken by a great many people. The daily total needed by the human body is estimated at 1 to 2 gm. This is required to produce the hydrochloric acid of the gastric juice and to maintain the almost constant level of salt in the blood and body fluids. An excess of salt is usually excreted by the kidneys rather promptly unless these are damaged by disease. There are many who believe that such an excess, if long continued, tends to injure the kidneys. Since the excessive ingestion of salt is due merely to habit, it is well to caution normal persons as well as sick ones against the abuse of the salt-cellar.

Certain patients with œdema are greatly helped by placing them on a salt-poor or salt-free diet. In many cases of nephritis the kidneys cannot

[1] *Nutrition and Clinical Dietetics*, 3d ed., Lea & Febiger, Philadelphia and New York, 1923.

excrete more than a few grams of salt a day. The remainder is held back in the body and, since the body jealously guards the osmotic pressure of its fluids, water is retained to dilute the salt. If we therefore decrease the salt intake below the level of the excretory power of the kidney the store of sodium chloride will be gradually eliminated, taking with it much water. Although a disappointingly small number of cases of œdema are due to this cause, it is well to try a salt-poor diet in dropsy. This causes much trouble to the dietitians and nurses and not a little discomfort to the patient, who misses the condiment to which he has become accustomed. A diet which contains practically no salt can be devised only with great difficulty. Such a salt-free diet has been advocated in hypertension but has not been widely adopted.

In certain cases of severe diabetes the diet is so greatly restricted that it contains practically no salt. This diminishes the water content of the body, increasing the tendency toward dehydration. Patients with severe diabetes seem to suffer greatly from the effects of dehydration, particularly if the blood and body tissues contain an excess of sugar, diacetic and beta-hydroxybutyric acid, which can be removed only by the kidneys. Such patients should be given large amounts of fluid, and many clinicians advise giving 5 to 10 gm. of salt daily in broths. This makes the patient thirstier and it helps to retain water in the tissues. It may produce a moderate œdema, but this is regarded by some as a favorable sign if coma is threatening.

Iodine.—Iodine, as a constituent of the diet, has recently attracted great attention. Marine[1] and his associates showed that endemic goitre (simple goitre) is caused by a lack of iodine in the food and drinking water. Such a deficiency occurs in those mountainous and inland districts where goitre and cretinism are prevalent. Near the seashore and certain other areas of the globe iodine is found in appreciable amounts in the water and vegetables because it is present either in the soil or in the air.

Iodine seems to be particularly important for women, especially at the age of puberty and during pregnancy. Marine produced a striking diminution in the incidence of goitre in school girls in Ohio by giving them twice during the year 2 gm. of sodium iodide in 0.2 gm. doses over a period of two weeks. Iodine may be given in chocolate tablets. Probably as small an amount as 1 gm. of sodium iodide twice a year is sufficient. Some have advocated that iodine be added to the water supplies of all communities in which goitre is common. This would be rather expensive and wasteful, since only a small fraction of the water is used for drinking. The general opinion seems to be that the best method is to require that all table salt in such regions should contain a certain amount of iodine. There is perhaps a slight danger in giving much iodine, since an excess of this substance sometimes changes a simple adenoma of the thyroid into a toxic adenoma.

Acids and Alkalies.—The blood and other fluids of the body are maintained at an extraordinarily uniform hydrogen-ion concentration in the neighborhood of Ph 7.35, which is just on the alkaline side of neutrality.

[1] Marine, D., and Kimball, P. O.: *Jour. Lab. and Clin. Med.*, 1917, **3**, 40; *Jour. Am. Med. Assn.*, 1921, **77**, 1068.

It is impossible within the limits of this article to discuss fully the elaborate mechanism by which this is maintained. The blood contains the buffer substances, the phosphates and proteins, which tend to hold an equilibrium. The acid radicles from the food and the carbon dioxide produced in the tissues can neutralize the bases. The basic radicles in the food, the ammonia in the urine, the calcium, magnesium, etc., from the bones can neutralize the acids.

The laity has a false idea regarding acid foods. According to their beliefs anything that tastes acid must act as an acid in the body. This is true for such inorganic acids as hydrochloric or sulphuric, but these are seldom taken except as medicine. The foods ordinarily called acid are those containing acetic acid, such as vinegar, and those containing citric acid, such as oranges, lemons, etc. As a matter of fact, acetic acid and citric acid are oxidized in the body. If they have been combined with bases these bases are liberated to act as alkalies.

The supposed acidity of certain foods causes much apprehension to many persons. They have been told that certain diseases, such as gout, arthritis, eczema, and sore gums, are caused by "too much acid in the blood." Therefore they avoid the foods which taste acid but act as alkalies. A more rational procedure is to scrutinize the actual reaction of the ash of the various foods, since it is only this ash that must be neutralized by the resources of the body. A table is reproduced from the work of Sherman and Gettler.

TABLE 10.—EXCESS ACID OR BASE IN REPRESENTATIVE FOODS IN TERMS OF NORMAL SOLUTIONS.*

Article of food.	Potential acid.		Potential base.	
	Per 100 gm.	Per 100 calories.	Per 100 gm.	Per 100 calories.
Succulent vegetables:				
Asparagus	....	....	0.8	3.6
Potatoes	....	....	7.2	8.6
Carrots (or beets)	....	....	10.8	23.7
Fruit:				
Cranberries	....	....	1.8	3.8
Pineapple	....	....	6.8	15.7
Nuts:				
Almonds	....	....	12.0	1.8
Walnuts	....	1.1		
Legumes	....	....	23.9	6.9
Cereal:				
Oatmeal (or wheat)	12.9	3.2		
Rice	7.8	2.5		
Lean meat	12.0	10.4		
Fish	7.8			
Milk	....	....	1.8	2.6
Cheese	....	1.2		
Eggs	11.1	7.5		

* Compiled from Sherman: *Food Products*, 1915. Sherman and Gettler: *Jour. Biol. Chem.*, 1912, **11**, 363.

The most important disturbance of the acid-base equilibrium occurs in severe diabetes. We have shown previously that fat is completely oxidized only when one molecule of glucose is metabolized at the same time as one molecule of fatty acid. In moderately severe diabetes none of the carbohydrate ingested as such can be utilized by the body. In severe diabetes even the glucose derived from protein is excreted also. As a result of incomplete oxidation, fatty acids are in part left at the intermediary stage of diacetic acid, which is largely converted into beta-hydroxybutyric acid. Circulating in the body, these tend to produce a change in the hydrogen-ion concentration in the direction of an acid reaction, but in order to prevent this disaster the body neutralizes them by combining them with bases, chiefly sodium and ammonia. This draws upon bicarbonate reserves, the chief substances which can hold carbon dioxide in the blood. As a result the carbon dioxide content and the carbon dioxide combining power of the blood are greatly diminished. The factors of safety are seriously threatened. Sometimes a withdrawal of bases, such as calcium and magnesium, from the bones may stay the process. Every available base is called upon. The clinician often seeks to aid the process by administering sodium bicarbonate or calcium or magnesium. This seems rational, but Joslin has obtained excellent results, in threatened coma without using alkalies, and we cannot neglect the weight of his opinion, backed by his great clinical experience and excellent judgment. The most rational method of combating such a diabetic acidosis is to decrease the fatty acid danger by decreasing the fat metabolism through undernutrition and suitable diet. Better still, we try to increase the glucose oxidation. This can be helped by the modern methods of treatment, especially by the administration of insulin. The keto-acids disappear in the fire of glucose oxidation.

We must remember that diacetic and beta-hydroxybutyric acid appear in every patient when the carbohydrate stores are nearly exhausted. Thus we find ketosis in starvation, in fever patients on low diets, in surgical patients after operation, etc. We must remember, moreover, that the ketones are not the only acids which occur in metabolism. Normal muscular contraction is accomplished through the breaking down of glucose to lactic acid. Ordinarily in mild exercise this is rapidly reconverted into glucose through the oxidation of carbohydrate and probably through the oxidation of fat also. In severe exercise Barr, Himwich, and Leobel have shown that a considerable amount of this lactic acid escapes into the blood and circulates in the blood for some time before it is absorbed and reconverted by the resting tissues. While it circulates it causes a distinct shift in the hydrogen-ion concentration in the direction of acidity. In fact, normal men, after a few minutes of severe exercise, may show a greater acidosis than is found in diabetic coma.

There is a good deal of confusion with regard to the term "acidosis." It is used by the profession and by the laity to designate not only the condition in which ketone bodies (acetone bodies) appear in the urine, but also the term is applied to various vague and uncertain conditions, such as those which are believed to be the result of too much uric acid or hyperacidity of stomach or digestive upset. It seems better to employ

the expression "ketonuria" to designate the appearance of abnormal amounts of acetone or diacetic (aceto-acetic) acid or beta-hydroxybutyric acid in the urine. "Ketosis" is the term that should be applied to their formation in abnormal amounts. When this has reached the stage of diminishing the bicarbonate in the blood we can speak of it as a "diminution of the alkaline reserve." The term "acidosis" should be restricted to that serious condition found when the alkaline reserve has been so exhausted that the hydrogen-ion concentration of the blood has definitely shifted toward acidity.

THE BASAL METABOLISM IN HEALTH

The basal metabolism is usually measured when the individual is at complete rest in the morning twelve to fourteen hours after the last meal. This is called "basal" by courtesy, since lower figures would probably be found if the subject were studied during profound sleep at three or four o'clock in the morning. This, of course, is impractical. Krogh has made the suggestion that we use the term "standard metabolism" for the conditions ordinarily employed. Boothby and Plummer have adopted the term "basal metabolic rate." The German expression is "Grundumsatz."

The basal metabolism is of clinical significance because it is remarkably constant for a given individual. Most normal men do not vary more than 10 per cent. from their average figure when repeated tests are made. The writer has been studied in the calorimeter at intervals between 1913 and 1924 and has never varied more than 7 per cent. from his average. In a similar fashion, if we study a large group of normal men of approximately the same age and height and weight it will be found that almost all come within 10 per cent. of the average for the group. Apparently the basal metabolism is one of the physiological "constants, resembling in its uniformity the body temperature, the blood-pressure, hemoglobin, etc. It represents the heat produced by the resting tissues plus the heat required by the heart, muscles of respiration, kidneys, and the active glandular organs. The metabolism of the resting tissues is probably proportional to the total protoplasmic mass, although this cannot be measured. The rate of metabolism is influenced to a certain extent by the adrenals, but the great regulator is the thyroid secretion. An increase in the adrenal secretion may cause a temporary rise in metabolism. A total removal of thyroid secretion will cause a decrease of about 40 per cent. It is doubtful if the other ductless glands influence metabolism directly, though they may do so indirectly through the adrenals and thyroid.

If we compare individuals of different sizes it will be found that those who are heavier give off more heat, but a man who weighs 200 pounds will not give off twice as much heat as a man who weighs 100 pounds. Height is a factor also. If we make a careful study of warm-blooded animals and of men of different sizes we find that all have about the same basal heat production per unit of surface area. This is shown in Table 11, taken from Armsby, Fries, and Bramen.

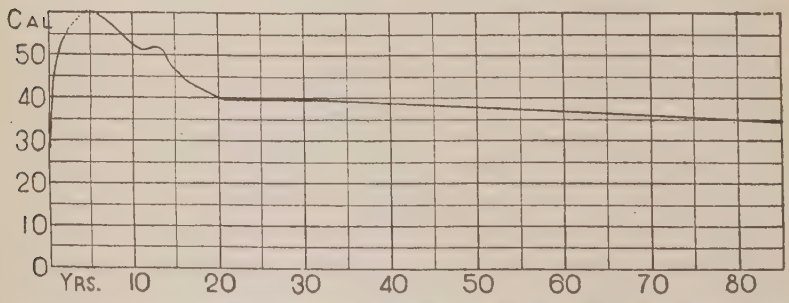
TABLE 11.—MEAN DAILY BASAL KATABOLISM PER SQUARE METER OF BODY SURFACE.

Species.	Basal katabolism calories.
Man (complete muscular rest), Benedict *et al.* (height-weight formula)	935 ± 5
Women (complete muscular rest), Benedict *et al.* (height-weight formula)	886 ± 6
Cattle (lying), Armsby *et al.* (Moulton's formulæ)	964 ± 24
Hogs (lying), Meissel *et al.*, Tangl, Fingering *et al.* (Meeh's formula) .	1078 ± ?
Horse (standing quietly), Zuntz and Hagemann	948 ± ?

To this we might add from Rubner's well known table the figure 969 for a goose and 1188 for a mouse. This relationship to surface area is not surprising when we remember the physical law that heat loss is proportional to the character and area of the surface. The animal organism, however, does not follow all the laws for heat loss which apply to inanimate objects. In the case of an animal the heat loss does not change greatly when the environmental temperature is lowered, say, from 30° to 20° C. Of course, an inanimate object would lose heat much more rapidly when the air was cooled. Probably the integument of animals protects the internal structures of the body to a considerable extent. This protection is limited, however, and cooling of the air beyond a certain point leads to shivering and the production of more heat, which keeps the body warm. Rubner believes that there is also a zone of chemical regulation in which the metabolism is increased without shivering so that the body is warmed by greater oxidations within the resting cells.

At any rate, there is ample proof that under similar physiological conditions and at ordinary room temperatures the metabolism of different men is proportional to their surface area. Perhaps this is due to the fact that the surface area is proportional to the protoplasmic mass.

FIG. 8



Curve showing the average calories per square meter per hour produced by males of different ages according to the estimations of Aub and Du Bois. The curve is probably too high between the ages of one and eighteen years.

If we determine the basal metabolism of a patient it is necessary to have some normal standard with which we may compare our results. Of course, the best standard would be the average obtained from a dozen or so normal individuals of the same age, sex, height, and weight, measured in the same apparatus under exactly similar conditions. This would involve great difficulties, so various laboratories have attempted to work out normal standards, utilizing the results obtained on normal controls studied by experienced technicians under the standard conditions of complete

muscular relaxation fourteen hours or more after the last meal. The large amount of material furnished by F. G. Benedict and his associates of the Nutrition Laboratory in Boston has served as the chief source of data. Aub and Du Bois in 1917 added to Benedict's cases some from various laboratories including their own, and suggested tentatively the standards given in Fig. 8 and Table 12.

TABLE 12.—SO-CALLED SAGE NORMAL STANDARDS. (AUB AND DU BOIS.) CALORIES PER SQUARE METER OF BODY SURFACE PER HOUR (HEIGHT-WEIGHT FORMULA).

Age, years.	Males.	Females.
14 to 16	46.0	43.0
16 to 18	43.0	40.0
18 to 20	41.0	38.0
20 to 30	39.5	37.0
30 to 40	39.5	36.5
40 to 50	38.5	36.0
50 to 60	37.5	35.0
60 to 70	36.5	34.0
70 to 80	35.5	33.0

The surface area of the patient is determined by means of a formula devised by Du Bois and Du Bois.

$$\text{Area (sq. cm.)} = \text{Wt.}^{0.425} \times \text{Ht.}^{0.725} \times 71.84.$$

This has been expressed in a graphic form which makes it possible to determine the surface quite readily. Boothby and Sandiford have changed this into a nomogram which is even simpler.

The surface area of children can be estimated from Lissauer's formula, $K\sqrt[3]{w^2}$, W being the weight in kilograms and K constant, ranging from 10 to 11.1 according to weight. Benedict and Talbot have published a table (Table 13) which makes the determination easy.

TABLE 13.—ESTIMATED BODY SURFACES FOR BODY WEIGHTS FROM 3 TO 40 KILOGRAMS. (BENEDICT AND TALBOT)

Body weight (without clothing), kilos.	Surface[1] estimated for boys, sq. m.	Surface[1] estimated for girls, sq. m.	Body weight (without clothing), kilos.	Surface[1] estimated for boys, sq. m.	Surface[1] estimated for girls, sq. m.	Body weight (without clothing), kilos.	Surface[1] estimated for boys, sq. m.	Surface[1] estimated for girls, sq. m.
3	0.208	0.210	16	0.711	0.686	29	1.086	1.048
4	0.252	0.255	17	0.740	0.714	30	1.110	1.072
5	0.292	0.295	18	0.769	0.742	31	1.134	1.095
6	0.330	0.333	19	0.797	0.769	32	1.159	1.119
7	0.388	0.388	20	0.825	0.796	33	1.183	1.142
8	0.424	0.424	21	0.853	0.845	34	1.207	1.164
9	0.459	0.459	22	0.879	0.872	35	1.230	1.188
10	0.492	0.492	23	0.906	0.898	36	1.254	1.210
11	0.524	0.534	24	0.932	0.924	37	1.277	1.233
12	0.556	0.566	25	0.958	0.949	39	1.300	1.255
13	0.586	0.597	26	1.009	0.974	39	1.323	1.277
14	0.616	0.627	27	1.035	0.999	40	1.345	1.298
15	0.645	0.657	28	1.060	1.024			

[1] Surfaces estimated, using formula $K\sqrt[3]{w^2}$; for values of K at the different weight ranges.

FIG. 9.

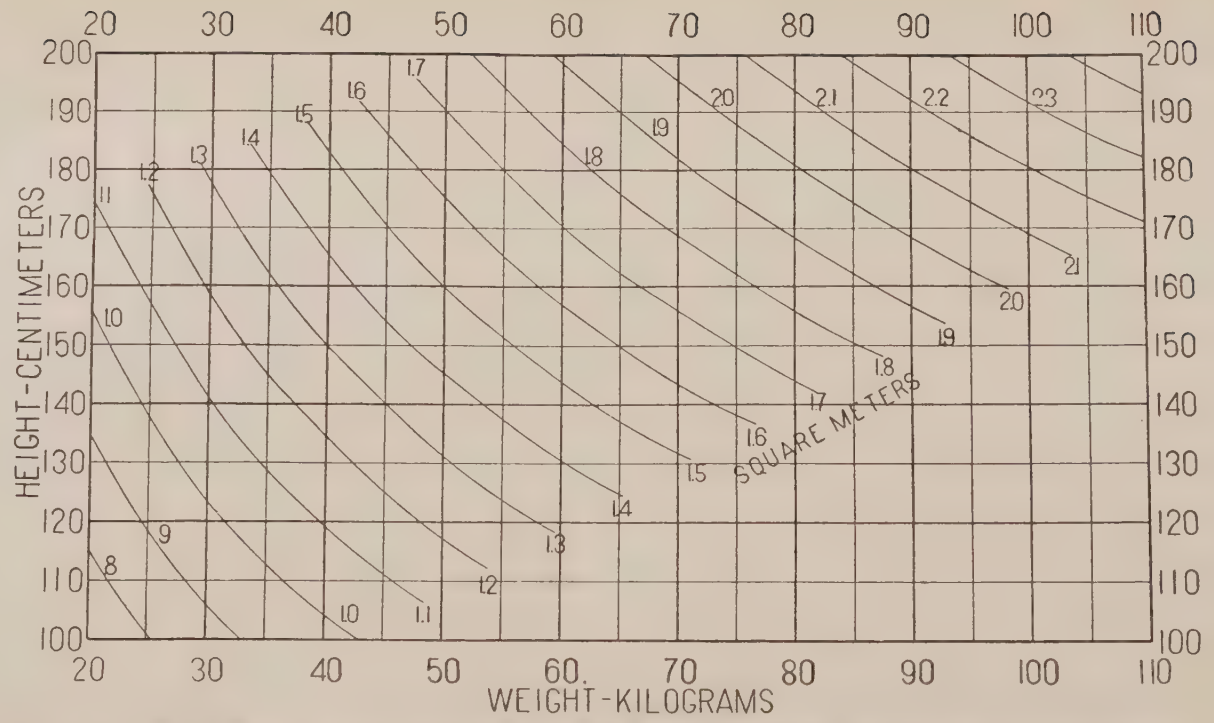


Chart for determining surface area of man in square meters from weight in kilograms (Wt) and height in centimeters (Ht) according to the formula: Area (sq. Cm.) = Wt. $^{0.425}$ × Ht. $^{0.725}$ × 71.84.

FIG. 10

Chart for surface area determinations. (Copyright, 1920, by W. M. Boothby and R. B. Sandiford.)

The metabolism per unit of surface varies with age, as is shown in Fig. 7 and the Table 13. The figures for females are about 7 per cent. lower than those of males for some reason that has not yet been satisfactorily explained. Possibly part of the difference is due to the greater proportion of fat in women. The difference, however, is established so early in childhood that the real cause remains a mystery.

Harris and Benedict in 1919 published their classical normal standards derived from the large number of normal controls studied at the Nutrition Laboratory. They approached the matter from a purely statistical method, using the biometrical method of correlation coëfficients in an exhaustive study of all the possible factors. They came to the conclusion that sex, age, height, and weight were the four important factors and evolved the following multiple prediction formulas:

For men

$$h = + 66.4730 + 13.7516w + 5.0033s - 6.7550a$$

For women

$$h = + 655.0955 + 9.5634w + 1.8496s - 4.6756a$$

in which h = total heat production per twenty-four hours; w = weight in kilograms; s = stature in centimeters; a = age in years. These sound complicated, but tables have been published so that their application is really quite easy.

Harris and Benedict were strongly opposed to the idea that the surface area had any causal relationship to the basal metabolism, though they recognized the fact that it furnished a good basis of comparison. It so happened that they employed the two factors, height and weight, which are used for determining the surface area. They also used the other two factors of age and sex that were employed by the Sage investigators. These four factors are given somewhat different values in the two sets of standards, but on the whole the differences are rather small. The main divergence lies in the lower level of the Harris-Benedict curves, the figures averaging about 4 per cent. lower than the Sage standards. This is probably due to the fact that Harris and Benedict used a larger number of trained subjects who could lie absolutely motionless during the rest which lasted ten to fifteen minutes. The Sage figures were raised by including controls studied in the calorimeter and it is almost impossible to lie absolutely motionless for two or three hours. It so happens, however, that the Sage standards come surprisingly close to the large number of normal controls studied by Boothby and Sandiford at the Mayo Clinic, using experimental periods of six to fifteen minutes. Apparently the average subject in his first few tests gives figures that are about 4 per cent. higher than would be obtained after a period of training in the procedure.

There are probably certain objections to both sets of standards. The Sage curves are perhaps too high at the period of puberty, since the level was based on a series of determinations made on a particularly athletic group of Boy Scouts. Benedict has also questioned the level in old age, as the subjects were not very numerous at this period of life. The Harris-

Benedict standards have been attacked on account of certain discrepancies due to statistical methods, particularly in the slope of the curves for the two sexes with advancing age. At the present time many of the clinical laboratories have followed Boothby in using the Sage standards. Krogh points out that these are probably more reliable for persons of exceptional build or higher age. He thinks, however, that they are too high for determinations on normal subjects under his strict rules of procedure. He has recently advocated the adoption of the standards given in Table 14 which are 6 per cent. lower than those of Aub and Du Bois.

TABLE 14.—STANDARD METABOLISM PER SQUARE METER PER MINUTE.

Age.	Calories. Men.	Women.
15 to 16	0.707	0.658
16 to 17	0.689	0.638
17 to 18	0.672	0.620
18 to 19	0.657	0.606
19 to 20	0.646	0.599
20 to 22	0.637	0.590
22 to 24	0.631	0.584
24 to 26	0.623	0.580
26 to 30	0.615	0.575
30 to 35	0.609	0.570
35 to 40	0.606	0.565
40 to 45	0.603	0.560
45 to 50	0.600	0.555
50 to 55	0.592	0.550
55 to 60	0.585	0.542
60 to 65	0.577	0.535
65 to 70	0.568	0.528
70 to 75	0.558	0.518

At the present time it seems advisable to compare a patient with all these normal standards. The discrepancies between them will serve to emphasize the fact that there is no fixed normal but rather a broad zone in which most of the results will fall.

Dreyer has also made a statistical study of the American controls and has eliminated the factor of height in the following formula:

$$H = \frac{\sqrt{W}}{K \times A^{0.1333}}$$

H = expected calories in twenty-four hours; W = net body weight in grams; C = total calories produced in hours; A = age in years; K = 0.1015 in males and 0.1129 in females.

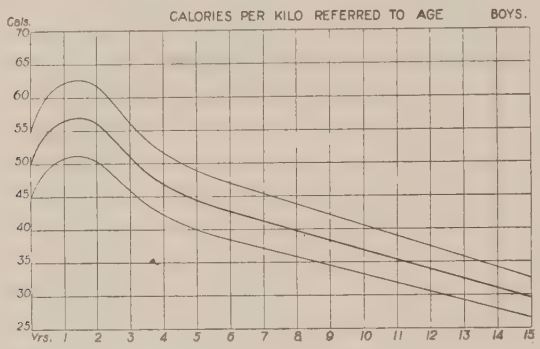
Although this may give an excellent average deviation in a statistical study of a large number of individuals, most of whom have ordinary body proportions, it does not seem safe to apply it to those who are thin or those who are fat. Dreyer's formula has not been used very much in this country, although it is often employed by the British laboratories.

The normal standards for children are even more difficult to establish. It is hard to secure absolute quiet and in the case of babies it is necessary to give food before the observations in order to induce them to sleep.

There have been numerous studies on infants, but the largest series has been presented by Benedict and Talbot and their associates. Talbot's curves, showing the normal average with the zone extending 10 per cent. above and 10 per cent. below this average, are given in Figs. 11 to 14.

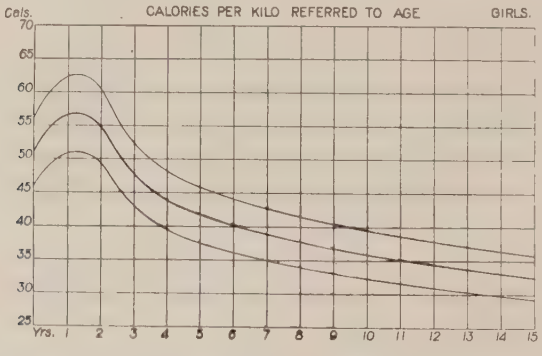
Talbot has found that premature infants show an exceedingly low heat production. Hasselbalch, Bailey, and Murlin demonstrated that the basal metabolism of the new-born infant is about the same as that of the

Fig. 11



Basal metabolism, calories per kilogram of body weight for twenty-four hours of boys at different ages. The curve is projected from twelve years upward. (Talbot.)

Fig. 12



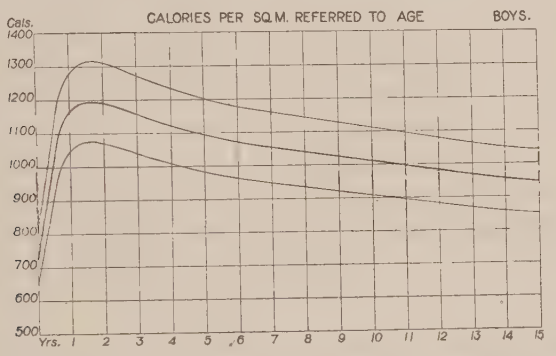
Basal metabolism, calories per kilogram of body weight for twenty-four hours of girls at different ages. The curve is projected from twelve years upward. (Talbot.)

adult according to surface area, but somewhat greater per kilogram of body weight. During the first year of life heat production rises very rapidly, perhaps as Krogh suggests on account of the development of muscular tone. The peak is reached in the second year, and at this time children radiate from each square inch of skin 30 to 40 per cent. more heat than the adult. Some children radiate from each unit of surface almost twice as much as old women. It is not surprising, therefore, that they stand cold weather so much better than adults and that men in the

prime of life stand it better than the aged. The skin of a child is warm; that of an old person cold. The internal fires burn fiercely in youth, feebly in old age.

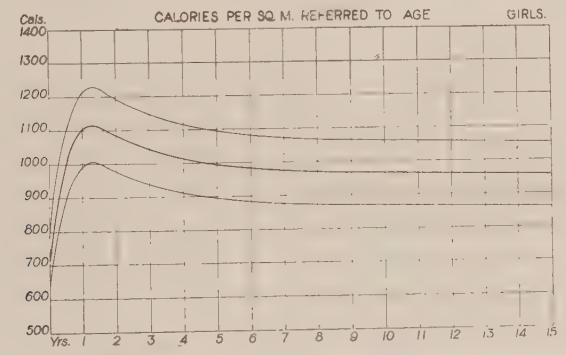
As childhood progresses there is a rapid fall in metabolism, though in some cases there seems to be a rise at the time of puberty when there is a change in the rate of growth and in the relationship of the ductless glands due to the development of the gonads. The Sage investigators

FIG. 13



Basal metabolism, calories per square meter of body surface for twenty-four hours of boys at different ages. The curve is projected from twelve years upward. (Talbot.)

FIG. 14



Basal metabolism, calories per square meter of body surface for twenty-four hours of girls at different ages. The curve is projected from twelve years upward. (Talbot.)

believed that they had established a rise in the curve at this period, but Benedict has disputed the matter vigorously. Further investigation is needed, and we are uncertain as to the normal levels between the ages of twelve and fifteen. There is also a lack of material at the period of menopause in women. Not many studies on old people have been published, but there are enough to demonstrate a gradual fall in metabolism after the age of forty. Between the ages of twenty and forty the changes are slight.

If we study any large series of normal controls we find that almost all of them give figures within 10 per cent. of the average normal, as estimated by the Sage or Harris-Benedict standards. A few show variations as great as 15 per cent. and in rare instances deviations up to 20 per cent. are encountered in subjects apparently normal. There seems to be but little change during the day, but there is evidence pointing toward a fall in metabolism during sleep and quite a marked diminution in heat production at the dead of night when sleep is profound and the body temperature low. The changes in body shape are taken care of by the estimation of the surface area and the allowances made for height and weight. With extreme undernutrition, however, the figures pass below the normal range. Normal figures are found in obese subjects unless the endocrines are affected. Differences due to race have not yet been established. Most normal women seem to show no definite changes with the menstrual cycle, but there is evidence that some show a rise of 10 or 15 per cent. in the premenstrual period.

With due consideration of the factors mentioned above, we can establish the relationship of the patients' basal metabolism to the average normal. This is usually expressed in terms of plus or minus the percentage above the average. If the figure is greater than +10 per cent. we suspect an abnormally high metabolism, but we cannot definitely say it is beyond the normal limits unless the figure is greater than +15 per cent. It is abnormally low if the figure is beyond the limits of −10 or −15 per cent. It is obviously necessary to scrutinize carefully all laboratory reports and make sure that the patient has been properly handled and that the technique has been faultless. Even a moderate degree of nervousness on the part of the patient or tactlessness on the part of the technician will cause a rise in metabolism. For this reason it is necessary to make duplicate or triplicate tests, and in most cases it is advisable to repeat the procedure on another morning. The clinician should scrutinize the agreement of the duplicates and should also examine the series of normal controls studied in the same laboratory. Every careful technician is glad to exhibit his series of normal controls.

The Total Metabolism.—We must remember that the basal metabolism represents the heat production only under the somewhat unusual conditions of complete muscular repose fourteen hours or more after the last meal. Ordinarily our patients are under these conditions for a comparatively short period of the day. During the rest of the time their oxidative processes are increased either by muscular activity or by the stimulating effects of food.

Specific Dynamic Action of Food.—Lavoisier, the founder of the science of nutrition, recognized the fact that food increased the metabolism. The subject was first studied intensively by Rubner, who introduced the term "specific dynamic action." He believed that a certain portion of each food was given off as extra heat which was wasted unless the body required this extra heat on account of the chilly atmosphere. Lusk, in a series of exceedingly careful experiments on dogs in a calorimeter, studied the question in detail and changed our views on the subject. In one dog, after the ingestion of 1200 gm. of meat, the heat production was

almost doubled from the second to the tenth hour, falling off gradually for the subsequent ten hours. This increase in total metabolism followed closely the curve of nitrogen elimination, which indicates the rate of protein metabolism. The extra calories produced by the dog were greater than could have been accounted for by the extra metabolism of protein, and some of the stored carbohydrate or fat was therefore oxidized. This showed that there was more than a mere waste of a portion of the protein. In tracing the matter further Lusk found that a stimulation was produced by the ingestion of certain amino-acids, such as glycocoll and alanin. Others, such as leucin and tyrosin, had slight effect, and glutamic acid none. He showed that the rise in heat production was not due merely to the oxidation of the amino-acids by giving glycocoll to a phlorhizinized dog. There was a marked stimulation of metabolism in spite of the fact that there was no oxidation of the amino-acid, since its entire energy content was eliminated in the form of sugar in the urine. The cause of the specific dynamic action of protein probably lies in a chemical stimulation of the cells by certain amino-acids or in the products of their intermediary metabolism. There is no specific dynamic action when protein is deposited in the form of new tissue. There is none following ingestion of bones, warm water, meat extract, urea or salt.

Carbohydrates cause a rise in metabolism, probably on account of a plethora of acetaldehyde molecules which, being present in abnormal amounts, stimulate the cells. When a dog is given 50 gm. of glucose, fructose (levulose), or sucrose, the metabolism is increased 30 to 37 per cent. in the second, third, and fourth hours. Similar results are obtained in man by giving large quantities of carbohydrate. The specific dynamic action of fat is much less marked. It manifests itself slowly on account of the slow digestion and never causes a large percentage increase. Murlin found that the stimulation of glucose could be superimposed upon that of fat. With man it is not possible to give the enormous amount of meat that can be swallowed in a few minutes by a dog. Aub and Du Bois induced an achondroplastic dwarf to eat chopped meat steadily for one hour. He consumed 662 gm. of beef, containing 23.2 gm. of nitrogen. In the next few hours his metabolism increased 46 per cent. above its basal level. The ingestion of 200 gm. of glucose by a normal man caused a rise of about 12 per cent. Benedict and Carpenter studied the effects of many different combinations of food. After ingestion of large amounts of beefsteak as much as 20 or 30 per cent. of the fuel value of the food may be given off as extra heat. This they call the "cost of digestion" for lack of a better term. In the case of ordinary meals the cost of digestion amounts only on the average to about 6 per cent. of the fuel value. If, therefore, we wish to estimate the total increase in metabolism caused by taking three meals a day we should add to the basal figures about 6 per cent. of the calories of the total food. It has previously been the custom to allow 10 per cent. for the specific dynamic action, but this figure is evidently too high unless the diet contains an unusual amount of protein.

In the Sage laboratories it was found that a small breakfast consisting of 30 gm. of bread, with 8 gm. of butter, and a cup of caffein-free coffee

containing 10 gm of sugar and 60 cc. of milk resulted in a rise of 5 or 10 per cent. of the total metabolism for one hour with no demonstrable increase after that time. Such a breakfast is therefore allowable two or three hours before a basal metabolism test in cases in which it is absolutely required to support the strength or morale of the patient. C. G. and F. G. Benedict[1] suggested a breakfast consisting of 1 cup (200 cc.) of caffein-free coffee, 16 mg. of saccharin, 30 gm. of medium cream and 25 gm. of potato chips. They found that this caused no significant rise in metabolism.

Richardson and Mason found that they caused an increase of only 2 per cent. in the metabolism if they gave diabetic patients every two hours a diet which exactly replaced food oxidized every two hours, as determined by fasting experiments. In this manner they furnished the cells the material required without any stimulating excess at any one time.

The Effect of Muscular Exercise.—A man can increase the heat production ten fold by severe muscular exercise. It is therefore necessary for us to consider the increases caused by bodily activity if we desire to find the total food requirement of a patient. Here is the weakest point in all metabolism work, and the errors may be as great as 20 to 50 per cent. A mere change of posture, with the slight muscular activity which accompanies sitting upright in a chair, increases the heat production about 5 or 10 per cent., the average increase being between 6 and 8 per cent. Standing with the body relaxed is accompanied by a slightly greater heat production, and standing stiffly at attention requires perhaps 15 or 20 per cent. more calories than lying relaxed. It is evident that the muscular effort is the factor responsible, since it was found in the Sage calorimeter that the heat production was very slightly altered by placing the subject in a comfortable steamer chair with his body inclined at an angle of about 45°. As a matter of fact, the average was 3 per cent. lower for the subjects in the semi-reclining posture. This shows us that we may employ back rests in patients seriously ill without increasing their metabolism and it has lent support to the practice of allowing tuberculous patients to use the semi-reclining posture while taking their cure outdoors. The results obtained in standing and sitting in an upright chair warn us to be careful when we first allow convalescents out of bed. It is quite certain that their metabolism increases as much as that of normal controls and it is quite possible that they require much more than the normal expenditure after their muscles have been weakened by a prolonged stay in bed. In normal men these slight increases in oxidation are accompanied by a proportional rise in pulse-rate. Clinicians have long recognized the importance of watching the pulse-rate in convalescents when they first get out of bed.

Walking at a slow rate may be accomplished with an increase of about 100 per cent. over the resting metabolism. Rapid walking on an incline may require 800 per cent. increase. Rapid bicycle riding can increase the heat production about nine or ten times. If such work is done on a

[1] A Permissible Breakfast Prior to Basal Metabolism Measurements, *Boston Med. and Surg. Jour.*, 1923, **188**, 849.

stationary bicycle ergometer it is possible to measure the kilogrammeters of work accomplished and calculate the energy required.

The muscles are extraordinarily efficient, especially those of the legs, and 25 to 33 per cent. of the calories may be transformed into work by a trained subject. With the untrained subject the efficiency is lower, and there is much evidence to indicate that it is very low in patients who are severely ill. This important question needs much further investigation.

It has been found in the Nutrition Laboratory in Boston that such a simple task as chewing gum or rubber may increase the metabolism 17 per cent. A girl engaged in typewriting performed her work at the expense of 24 calories per hour. Various other factors have been studied, and we could perhaps watch a patient carefully, record the number of minutes spent in various activities, and estimate the extra expenditure of energy. There would still be a great uncertainty regarding the muscular efficiency. We need a large number of studies of patients living in respiration chambers, but such investigations are extremely scarce.

With patients who are well enough to be up and about we may, for lack of better figures, assume that their muscular efficiency is normal and compare them with normal individuals engaged in about the same occupations. Such a table, based on dietary studies, has been given on page 79. The Interallied Scientific Food Commission adopted Lusk's coëfficients in calculating the diet of the average man and the percentage of this standard allowed for women and children.

TABLE 15.

	Calories.	Relative food needs.
"Average man," fourteen years and older	3,000	1.00
"Average woman," fourteen years and older	2,500	0.83
Boy or girl, ten to fourteen years old	2,500	0.83
Boy or girl, six to ten years old	2,100	0.7
Boy or girl, naught to six years old	1,500	0.5
Total for such a family of five	11,600	
Ten per cent. allowance for waste	1,160	
	12,760	
Calories per "person," per day	2,524	
Calories for the family, one week	90,000	

The figures given for normal men have been based on field studies made by measuring the food consumed by persons in approximate weight and nitrogen equilibrium. If the studies are continued over a long enough period of time we are justified in assuming that the food consumption has actually balanced the requirement. If we apply this method to patients who are severely ill we are met with a great many difficulties. The nitrogen-balance and weight equilibrium are influenced by many pathological factors. Thus, Coleman and Shaffer, and Coleman and Du Bois found that it was necessary to give typhoid patients about twice as many calories as they actually expended before they could be brought into nitrogen equilibrium. In hyperthyroidism, Boothby and Sandiford were forced to supply a large excess of calories above the basal in order to attain nitrogen-balance. This is largely accounted for by the fact

that in exophthalmic goitre the performance of a given amount of work requires about twice the expenditure of calories that it does in a normal individual.

The writer has been repeatedly asked to estimate the number of calories required by patients with various diseases. He has attempted to answer the questions by considering the result obtained in a large number of calorimeter experiments and observations in the metabolism ward extending over a period of more than ten years. Each year the question seems to be more difficult. It is impossible to give a table of various diseases showing the optimum diet for patients of varying sizes and ages. The best he can do is to calculate the expected basal metabolism according to sex, age, height, and weight and the specific disease with due regard to its severity. To this basal figure we may add 6 per cent. for the specific dynamic action of foods, a similar amount for losses in the feces, and about 25 per cent. for muscular activity if the patient is confined to bed. If the patient is up and about we may use some such method of calculation as is found in Table 16, taken from Lusk.

TABLE 16.

Occupation.	Calories.
In bed twenty-four hours	1,680
In bed eight hours, work involving sitting in a chair sixteen hours	2,170
Bed eight hours, in a chair fourteen hours, moderate exercise two hours	2,500
Farmers	3,500
Rider in a six-day bicycle race	10,000

Once we have estimated the expenditure of energy, we must decide whether or not we want to employ undernourishment or overnourishment. We must also take into account the specific diseases and the limitations of the appetite.

The Vitamines.—It has long been recognized that a diet containing a plentiful amount of protein, fat, and carbohydrate might lead to scurvy if certain constituents found in fresh fruits or vegetables were lacking. We did not appreciate the nature and importance of such deficiencies until the work of Eijkmann, in 1897, F. Gowland Hopkins, in 1906, and Funk, who in 1912 coined the word "vitamine," or according to the more recent spelling "vitamin." In the last ten years our knowledge of these substances has grown with leaps and bounds, and they have assumed perhaps an undue prominence in nutrition. None of the discoveries regarding vitamines has diminished the importance of the proteins, fats, and carbohydrates. The discovery of a new lubricating oil would not diminish the importance of coal or gasoline.

At the present time we recognize three main classes of vitamines. The first, usually called "fat-soluble A," occurs particularly in certain fats and green plants. Lack of this vitamine results in cessation of growth and a disease of the eyes called "xerophthalmia." The second, water-soluble B, is widely distributed in animal and plant foods, especially in the outer coatings of seeds. If absent from the diet there is cessation of growth and polyneuritis or beriberi. The third, water-soluble C, is the antiscorbutic vitamine found in fresh plants and fruits. Table 17 shows the distribution of these vitamines in the more important foodstuffs.

TABLE 17.—ESTIMATED DISTRIBUTION OF VITAMINES IN CERTAIN FOOD MATERIALS.[1]

Source.	A.	B.	C.
Protein rich foods:			
Milk[2] and milk products			
Milk	++	+	+
Condensed	+	+	*
Evaporated	++	+	—?
Dried, whole	++	+	+
skim	+	++	+
Skimmed milk		+	+
Dairy products[1]			
Butter	+++	—	—
Buttermilk	+	++	+
Cream	++	—	+
Cheese	+	*	*
Cottage cheese	+	*	*
Eggs:			
Eggs	++	++	+?
Yeast:			
Yeast	?	+++	—
extract	?	+++	—
Meats and Fish:			
Brains	+	++	*
Fish, lean	—	Slight	*
fat	+	Slight	*
Heart	+	+	+?
Kidney	++	+	+
Liver	++	++	+
Meat (muscle)	+	+	+
extract	—	—?	—
canned	—	Slight	—
Roe, fish	+	++	+?
Sweetbreads	+	++	*
Nuts:			
Almonds	+	+	*
Brazil nuts	—?	++	*
Chestnut	*	+	*
Cocoanut	+	++	*
press cake	+	++	*
Filberts	*	++	*
Hickory	*	++	*
Peanuts	+	++	*
Pecans	*	+	*
Pine nuts	+	+	*
Walnuts, black	*	++	*
English		++	*

[1] Taken with modifications from the table in Sherman and Smith, The Vitamines, Monograph Series, *Am. Chem. Soc.*, which is based on the table presented by the British Medical Research Committee, Report 38. (From Carter, Howe and Mason, *Nutrition and Clinical Dietetics*, Lea & Febiger, 1923, and from Eddy, The *Vitamine Manual*, Williams & Wilkins, 1922.)

[2] The vitamine content of milk and milk products is variable—according to the diet of the cow and the mode of handling and treating. This is particularly true of vitamine C.

Source.	A.	B.	C.
Carbohydrate-rich Foods:			
Grain:			
Barley, whole	+	++	—
Bread, white (water)	?	+	—
white (milk)	+	+	?
whole wheat (water)	+	++	?
whole wheat (milk)	++	++	?
Corn (maize), white	—	++	—
(maize), yellow	+	++	—
Cottonseed meal	+	++	*
Flour, white	—	—	—
Grains, sprouted	+	++?	++
Malt, green	+	++?	++
Millet	++	++	*
Oats	+	++	—
Rice, polished	—	—	—
whole grain	+	++	—
Rye, whole	+	++	—
Wheat embryo	++	++?	—
Endosperm	—	+	—
Middlings, commercial	*	+++	—
Bran	+	++?	—
Whole	+	++	—
Sugars and Starches:			
Glucose	—	—	—
Honey	—	+	—
Starch	—	—	—
Sugar	—	—	—
Water and Salt-rich Foods:			
Fruits:			
Apples	+	+	+
Bananas	+?	+?	+
Cloudberries	*	*	+++
canned	*	*	+++
Cocum (dried)	*	*	+
Grape juice	*	+	+
Grapefruit	*	++	++
Lemon juice	*	++	+++
dried	*	++	+++
Limes	*	+	++
Mango	*	*	+
Orange juice	+	++	+++
peel	+	+	++
Pears	*	+	*
Prunes	*	+	—
Raspberries	*	*	+++
canned	*	*	+++
Tamarind, dried	*	*	+
Tomatoes, raw	++	+++	+++
canned	++	+++	+++
dried	++	+++	++
Vegetables:			
Alfalfa	+++	+++	*
Asparagus	*	+++	*
Beans, kidney	*	+++	*
navy	*	+++	—
soy	+	+++	—
sprouted	*	*	++
string, fresh	++	++	++

Source.	A.	B.	C.
Vegetables:			
Beets	*	+	*
Cabbage, fresh, raw	++	+	+++
cooked	+	+	+
dried	+	+	+
green	++	++	++
Carrots, fresh, raw	+	++	+
cooked	+	+	+
Cauliflower	+	++	+
Celery	*	++	*
Cress	*	*	+
Chard	++	+	*
Cucumber	*	+	*
Dandelion greens	++	++	+
Dasheens	—?	+	+
Eggplant, dried	*	++	*
Endive	+	*	+
Legumes, sprouted	*	*	++
Lettuce	++	+	+
Onions	*	++	++
Parsnips	—?	++	*
Peas	++	++	+?
sprouted	*	*	++
Potatoes, sweet	++	+	*
white, raw	+	++	++
white, boiled (15 minutes)	*	+	++
white boiled (1 hour)	*	+	+
white baked	*	+	+
Radish	*	+	*
Rhubarb	*	*	+
Rutabaga	—?	++	+++?
Sauerkraut	*	*	—?
Spinach, fresh	+++	++	*
dried	+	++	*
Squash, hubbard	++	*	*
Swede	*	*	+++
Turnips	—?	++	*
Fat-rich Foods:			
Fats and oils:			
Beef fat	++	—	—
Butter[1]	+++	—	—
Cocoanut oil[1]	—	—	—
Cod-liver oil[1]	+++	—?	—
Corn oil	+?	—	—
Cottonseed oil	—	—	—
Fish oils[1]	++	—	—
Horse fat	+	—	—
Lard	—	—	—
Linseed oil	—	—	—
Margarine, nut	—	—	—
Oleomargarine	—	—	—
Mutton fat	++	—	—
Olive oil	—	—	—
Oleo oil	+	—	—
Orange-peel oil	++	*	*
Palm oil	+	—	—
Peanut oil	—	—	—
Pig kidney fat	++	—	—
Whale oil	++	*	—

[1] Antirachitic vitamine present.

We have described previously the methods by which the vitamines have been studied. Their importance for growth has been well demonstrated by Osborne and Mendel, McCollum and others, using young white rats as experimental animals. The clinical manifestations of lack of vitamines appeared in various famine districts of Europe since the Great War. In this country we seldom encounter diseases due to lack of vitamines except the scurvy of infants, rickets and pellagra. It is difficult in American cities to find an adult who is consuming a diet dangerously low in vitamines, although there are certain food cranks or patients with stomach disease who acquire scurvy by abnormal diets. There is nothing at the present time which points toward any particular benefit derived from an excess of vitamines over and above the amount required to prevent disease. Possibly some such benefit may be demonstrated at a later date and it therefore behooves us to be sure that our patients are well beyond the danger zone.

The prevention and cure of the various diseases caused by lack of the accessory food factors is discussed elsewhere. It may be well, however, to review some of the more important facts, following the excellent summary given in the report of the British Medical Research Committee. Beriberi is not caused by mere shortage of food. In fact, poverty usually insures that the whole grain is consumed, and beriberi will probably never appear as long as the population eats whole meal flour from rye, wheat, barley, maize, or consumes peas, beans, and lentils. These all contain the antineuritic vitamine, which is also found in eggs, yeast, liver, and brain. The disease is common only where the inhabitants subsist chiefly on polished rice.

If, as a result of a poor food supply, there is a deficiency of the fat-soluble vitamine A, there will be a retardation of the growth of children and perhaps war œdema and a disease of the eye called "xerophthalmia." The best preventives are milk, butter, cod-liver oil, and green leaves in such vegetables as cabbage. The vitamine is not appreciably affected by steaming for a few minutes and there seems to be only moderate loss when full cream milk is dried. In famine districts every effort should be made to give the children a sufficient amount of butter fat.

The British writers believe that *rickets* is caused by a lack of vitamine A. The disease certainly occurs most frequently when this vitamine is deficient, but the more recent work, particularly in America, points to its cause being a lack of sunshine or a deficiency of some special factor which happens to be present in large amounts in cod-liver oil.

Scurvy in infants is usually prevented by giving fresh orange juice or tomato juice, either fresh or from canned tomatoes. The British Committee suggests as a substitute for famine districts juice expressed from grated turnips or swedes. Such juices are necessary because milk is rather deficient in the antiscorbutic vitamine. Scurvy may occur even in nursing babies if the mothers have been receiving a diet deficient in the vitamines. It is not infrequent on long ship voyages and exploring expeditions. The antiscorbutic vitamine is rather easily destroyed by heating in an alkaline medium. Orange juice and tomato juice resist high temperatures fairly well, probably on account of their acidity. Most

canned and dried vegetables are useless for the prevention of scurvy. The lime juice required for so many years on British ships is inferior in value and lemon juice is much better. As a matter of fact, the original "lime juice" of the early part of the nineteenth century was really the juice of lemons. Fresh meat has some antiscorbutic value; preserved meats none. One of the best means of preventing scurvy is the use of germinated seeds. If wheat, barley, rye, peas, beans, or lentils are soaked in water for twenty-four hours and then kept moist, with access of air for a few days, they will sprout and develop a large amount of vitamine C.

The relationship of *pellagra* to the vitamines is still under dispute. The disease occurs on restricted diets and these diets are low in vitamines. We do not yet know which substance is the most important factor.

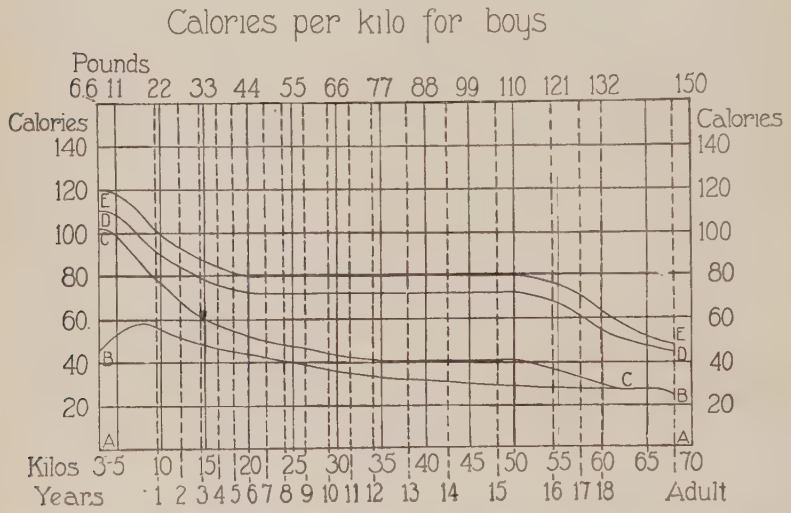
Vitamines A and B are absolutely necessary for the growth of the young, and perhaps they are also essential for the reconstruction of tissue in convalescents, though I am not familiar with any experiments bearing upon this question. We must not forget that the growing organism also needs certain mineral salts and a sufficient supply of the amino-acids found in the better class of proteins. We have previously discussed the lack of growth on such proteins as zein or on gelatine, which are deficient in some of the essential "building stones." It is rather easy to confuse the lack of growth caused by avitaminosis and that which is caused by lack of proper protein. In medical practice our patients are seldom placed upon a restricted diet for periods long enough to cause any symptoms from lack of vitamines. Milk, which is the basis of most diets, is rich in fat-soluble A and contains small amounts of water-soluble B and the antiscorbutic factor C. Orange and lemon juice, which are almost universally allowed, contain large amounts of antiscorbutic C. Egg-yolks contain large amounts of A, small amounts of B. Studies on egg-white seem to be lacking. Pure sugars, of course, contain no vitamines. Bread and cereals contain practically none unless the whole grain has been used. A diet of a liter of milk a day is deficient in antiscorbutic properties. The same may perhaps be said of the Lenhartz diet for gastric ulcer. All the gastric ulcer diets avoid the acid fruits and green vegetables, since these irritate the ulcer.

Metabolism During Growth.—The growing fetus tends to develop at the expense of the maternal tissues if there is a deficiency in the diet of the mother. In spite of this tendency, however, the fetus may suffer when the mother's food contains an insufficient supply of calories or proteins or mineral or vitamines. The mother needs an extra supply of all of these. During pregnancy the basal metabolism is not affected in the early months, but is increased slightly per unit of body weight in the latter months. On the other hand, the total requirement may be diminished through a curtailment of the usual household activities, although a given amount of work is probably performed with an abnormal expenditure of calories. It is well for the attending physician to see that there is no undue increase in the deposits of body fat as a result of overeating. Nursing mothers must be allowed extra food for the production of milk, and this must contain an adequate supply of vitamines and of

salts, particularly calcium. This is most easily supplied in the form of milk, thus transferring the need for calcium to the cow. Unfortunately, in cases of failing milk supply our efforts to increase the milk by giving the mother larger amounts of food are usually unsuccessful, resulting in a deposit of fat in the mother's body rather than an increasing activity of the lacteal glands.

We have already given the curves which show the basal requirements of children. For the first few years of life these include the stimulating effects of food. When the baby cries the metabolism is increased 40 per per cent. or more and when he begins to crawl and walk the requirements are much higher. There is also a requirement for growth and particularly a need for proteins of the better class, such as are found in milk,

FIG. 15



The solid vertical lines indicate weigh in kilos; the broken lines, approximate weights at each year of age. The space between lines *AA* and *BB* shows allowance for basal metabolism; between *BB* and *CC*, that the growth; between *CC* and *DD*, that for muscular activity between *DD* and *EE*, food values lost in excreta. The space between the lines *AA* and *EE* shows the total caloric allowance per kilo. (Holt and Fales.)

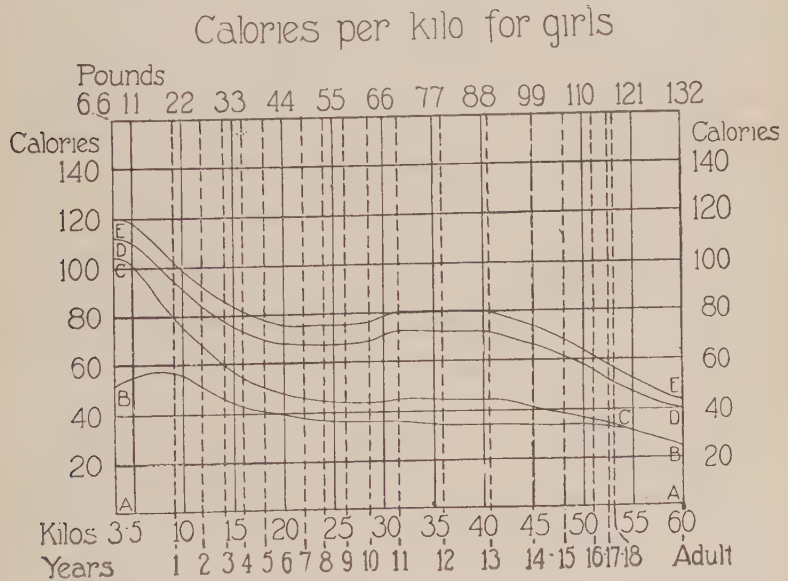
meat and eggs. A certain amount must be allowed for losses in the excreta. If we add all these factors we are able to calculate the total calories required in the food. This has been done by Holt and Fales in Figs. 15 and 16.

In using these charts it is well to remember that the largest factor after the age of three years is the bodily activity. For instance, Gephart found that the boys of St. Paul's School required about 5000 calories a day. Perhaps the best method of regulating the amount of food is to follow the body weight at frequent intervals and make sure that the child is gaining normally. The relationship of height and weight should be compared. Emerson believes that any child 7 per cent. under-weight is to be considered as undernourished.

We dread obesity in adults but not in children. Over-weight children are said to have a better life expectancy than the average. Excessive obesity is rare except in pituitary disease. Moderate obesity in children is easily cured by restricting the food. Ordinarily it is safe to let the child eat as much as he wants provided that the food is simple, of good quality and is not taken in snatches between meals.

Some few children are sensitized to certain foods and such idiosyncrasies will be discussed in other places. This sensitization is probably due to the absorption of a small amount of unchanged protein by the intestinal tract. Practically all protein is broken down by the digestive juices into products, such as the amino-acids, which are beyond the stage in which they can cause anaphylactic phenomena. In certain cases,

FIG. 16



The vertical and curved lines have the same significance as in Fig. 15. (Holt and Fales.)

however, small fractions of proteins pass into the blood retaining all their specific properties. Various phenomena, such as asthma, urticaria, and digestive disturbances, may follow just as in protein sensitizations produced parenterally.

THE REGULATION OF BODY TEMPERATURE

There is an intimate connection between the metabolism and the regulation of body temperature. Body heat is maintained at a constant level in temperate climates only through the production of heat within the tissues. Even a dead body gives off 500 to 1000 calories in twenty-four hours. It is therefore evident that the living body, with its circulation of blood in the subcutaneous tissues, must radiate larger amounts of heat.

Civilized man diminishes radiation by warm clothing. The face and hands are exposed to the room temperature, but the remainder of the surface has an entirely different environment. The temperature of the skin depends upon the temperature of the air beneath the clothing and also upon the amount of blood that is circulating near the surface. In cold weather or in the chill which accompanies the onset of a malarial paroxysm the body is able to diminish greatly the blood supply to the surface. This changes the skin into a leather suit. If the blood supply to the subcutaneous tissues is also diminished this leather suit is then provided with a nice lining of fat, which is an excellent material to prevent the loss of heat. Thus the cooling surface of the body is shifted inward and the warm internal organs lose heat to the cool inner surface of the subcutaneous tissues, which in turn pass it outward slowly to the surface.

In this manner a moderate cooling of the atmosphere may be taken care of without any increase above the basal heat production. If the cooling be too great for this simple regulation there will be an involuntary increase in heat production due to shivering unless this is forestalled by a voluntary exercise, such as beating the arms or stamping the feet. Perhaps there is a chemical increase also due to some unknown factor which causes the fires to burn more brightly in the cells. At any rate, the heat production is increased and the body temperature maintained in spite of the cold.

The level at which a sense of cold with shivering begins depends to a certain extent upon the degree to which the individual has been inured to cold weather. For ordinary mortals it depends upon the total metabolism at the time of exposure. An old man with a low basal metabolism will feel the cold much more than a child with a high metabolism. A woman with myxœdema will feel it more than a patient with hyperthyroidism. A fasting man sitting quietly in a chair will shiver in an atmosphere which would be comfortable if his metabolism were raised by muscular exercise or by the specific dynamic action of a large protein meal.

Another factor of great importance in the chill is the direction in which the body temperature is traveling. During the very first stages of a malarial paroxysm the temperature regulating centre is suddenly set at a higher level, say at 40° C. The body temperature is only 37° C. and it is therefore 3° cooler than it should be. The patient feels very much like a normal man whose temperature has been reduced to 34° C. by exposure to cold water. He is miserably cold. He shivers and shakes, and produces by means of muscular exercise enough heat to warm the body up to the point called for by the new conditions of heat regulation.

Once the body has been warmed enough to satisfy the new level of the heat regulating centre there is no more need for excessive heat production and the shivering is automatically stopped. The patient then feels comfortable except for the exhaustion caused by the exercise and the general discomfort of fever. In the last phase of the malarial paroxysm conditions are reversed and the temperature regulating centre is gradually set at lower and lower levels. The body which has reached 40° C. is now too warm. Heat is dissipated as rapidly as possible through radiation.

The blood flows through the skin near the surface and is thus exposed to the temperature of the air beneath the clothing, which is made as scanty as the nurse will permit. The normal vaporization of water is then increased by the outbreak of sweat and the percentage of heat removed in this fashion rises far above its normal figures. After several hours of such cooling the body attains the normal level of temperature.

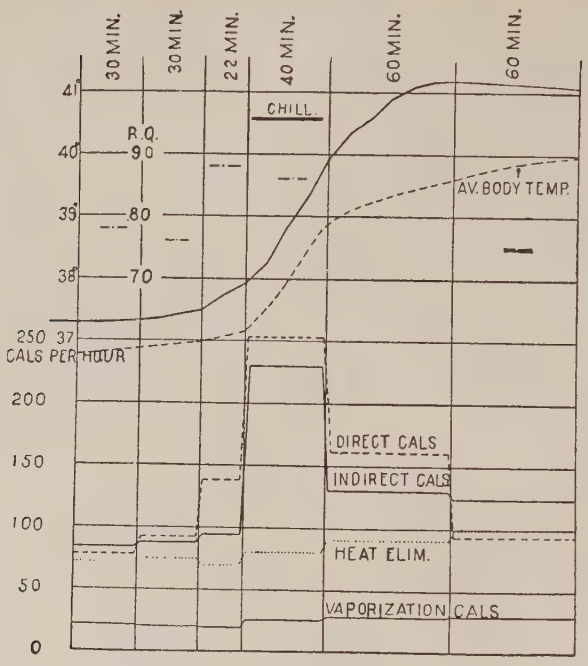
The various phenomena of malarial chills illustrate so well the regulation of body temperature that they have been studied by many investigators, notably Liebermeister and the Russians, Likhatscheff and Avroroff. Barr and Du Bois were able to follow the process in detail in the calorimeter of the Russell Sage Institute of Pathology. This apparatus is so accurate that Barr was able to devise a new method of calculating the amount of heat stored in the body and the average change in body temperature as opposed to the change in the mouth or rectal temperature. Studies made in various fevers have proved that the deep rectal temperature, even though measured every four minutes by a rapid, sensitive electrical thermometer, does not always indicate the average change throughout the body. Every clinician knows that the arms and legs may be growing colder while the rectal temperature rises. The measurement of such local changes is not possible if we have to rely solely on thermometers.

Barr's method is simple if we remember the laws of physics and the principles of the respiration calorimeter. The method of indirect calorimetry, based on oxygen consumption, gives us the total heat production. The total heat elimination is measured directly by the calorimeter and is the sum of the calories lost by radiation, conduction, and vaporization. If the total heat production for a given period exceeds the total heat elimination there must, of course, be a storage of heat within the body. Suppose in a given hour 40 calories are thus stored in a man who weighs 70 kilograms. The specific heat of the body is usually assumed to be about 0.83, and this means that the 70 kilograms of man are equivalent thermally to 58.1 kilograms of water. If we store 40 calories in 58.1 kilograms of water we raise its temperature 0.69° C. Therefore in this case the average temperature of the 70 kilogram subject must have been raised 0.69° C.

In Fig. 17 we see the results obtained on the malarial patient, G. S. His chill, which fell in the fourth period of the experiment, was violent and his heat production rose sharply from 86 calories to 230 calories an hour. The heat elimination was scarcely changed at all. Therefore he stored heat in his body at the rate of about 144 calories an hour. Both rectal and average body temperature rose sharply, but during the next period the body temperature change lagged behind the temperature rise in the rectum. The mechanism of the fall in body temperature is shown in Fig. 18 taken from a similar observation made on a similar chill following the intravenous injection of foreign protein. As soon as the temperature regulating centre was set at a lower level the elimination of heat increased rapidly until it exceeded the heat production. This of course withdrew heat from the body, causing a fall in temperature.

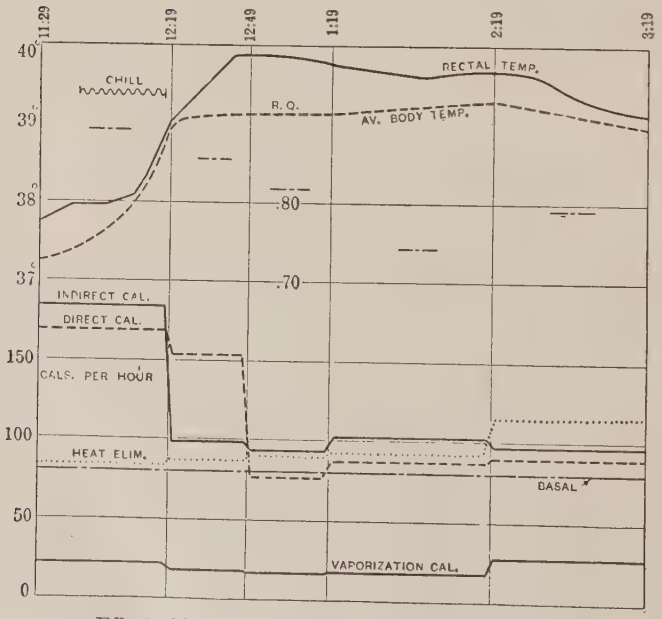
In order to demonstrate the true nature of the malarial paroxysm and

FIG. 17



Malarial patient, G. S., metabolism during chill.

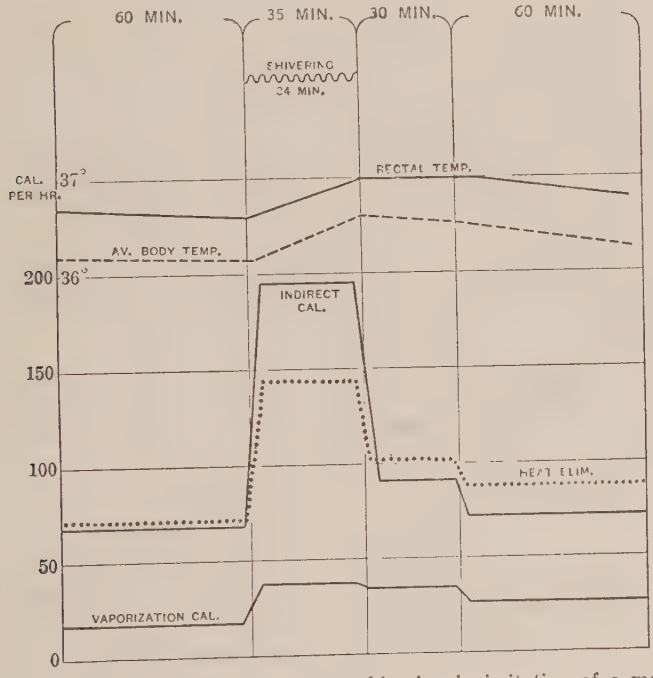
FIG. 18



Effect of intravenous injection of foreign protein.

the chill following the intravenous injection of foreign protein the writer went into the calorimeter and shivered for thirty-four minutes, imitating as carefully as possible the malarial patient. Fig. 19 shows that he produced about the same amount of heat as the patient, but his temperature rose only the fraction of a degree *because the heat elimination increased in proportion to the heat production.* His heat regulating centre had not been set at an abnormal level. His skin became warmer and warmer when he shivered; the malarial patient's skin became colder.

FIG. 19



Calorimeter experiment on a normal man, shivering in imitation of a malarial chill. After a period of sixty minutes he shivered violently for thirty-five minutes, and then remained quiet. The heat production rose sharply, the temperature scarcely rose at all. The dotted line shows heat elimination, the continued line heat production by the method of indirect calorimetry.

It is well to recall one simple fact regarding the vaporization of water established by von Willebrand in 1902 and since then rediscovered at frequent intervals. The skin at ordinary temperatures does not use the sweat glands, but the water vaporizes from its surface just as it would from a piece of meat. Sweat appears only when the air temperature rises above a certain point or when an excessive amount of heat must be eliminated or when there is a sudden nervous impulse such as fear.

Bearing in mind the results of the calorimeter experiments, we can explain a great many clinical symptoms. A warm skin means an increased heat elimination. It may be found in a fever patient who is maintaining his temperature at a level above the normal. It may be found in a patient

whose basal metabolism is high or whose total metabolism is raised by exercise. It may be found in any patient whose temperature is falling. The skin is moist if the increase in heat elimination is great; the skin is sweating profusely if the elimination is excessive.

A cold skin shows that the body is trying to conserve its heat. This may be due to a low metabolism, to a cold atmosphere, or to the necessities caused by a rising body temperature.

The rectal temperature does not always indicate accurately sudden changes in the average body temperature. There is often a tendency for the outlying parts to lag behind rapid fluctuations of the interior of the body.

There is another point on which the writer can testify from personal experience. The muscular effort of shivering thirty-four minutes can tire a man in fairly good physical condition and leave his body sore. The drenching sweat which follows a sudden fall in temperature must be exhausting also. It is well to remember these facts when we imitate malarial chills by giving foreign proteins intravenously. The metabolic phenomena of malaria are copied in the chills which follow such intravenous therapy.

In most fevers the rise of temperature is so gradual that there is no need for a chill. The heat production is increased enough above the heat elimination to allow the storage of, say, 10 to 20 calories an hour. This apparently is accomplished by maintaining the elimination at a constant level while the production increases either as a result of the higher body temperature or as the result of some unknown stimulus. Such a rise of temperature has been studied by Coleman and Du Bois in about a dozen cases of typhoid fever. In every case but one the heat elimination either remained constant or showed a slight rise, just as it did during the chills of malaria. We must therefore abandon the old theory that the temperature rises because the body diminishes the loss of heat. There is no actual diminution, but there is a relative diminution in the sense that elimination fails to keep pace with production.

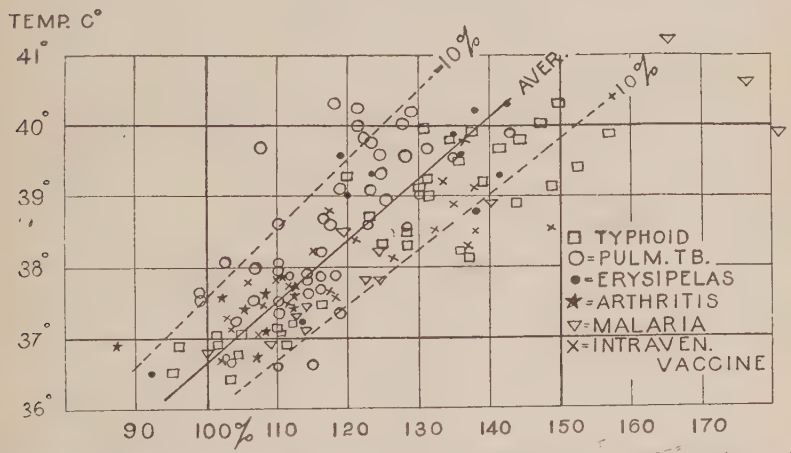
In the previous paragraphs we have spoken frequently about the heat regulating centre. Physiologists believe that such a centre exists, but the literature is filled with poor experimental work and conflicting theories. We can, however, be certain that injuries to some areas in the mid-brain are accompanied by fever. The origin of fever in the infectious diseases is still uncertain. Probably it is associated with the proteins from the bacteria or the body cells or else their products. Just why these should raise the temperature instead of depressing it we do not know. We are still uncertain as to whether or not fever is of beneficial nature, helping the body to fight infection. There is evidence which indicates that the higher temperature aids the antibodies, since most chemical reactions take place more rapidly at higher temperatures. It is just as well for the practitioner to consider some of these possibilities before he uses antipyretics to depress the temperature.

Many different fevers have been studied by various types of respiration apparatus and almost all observers have noted an increase in basal metabolism. The surprising uniformity in various diseases was first brought

out when a chart was made (Fig. 20) showing all the fever patients studied in the Sage calorimeter under uniform conditions. The increase in the metabolism was plotted against the increase in rectal temperature, and it was found that in all the fevers a rise of 3° C. caused an increase of about 40 to 50 per cent. in heat production. In pulmonary tuberculosis, which is accompanied by a slighter increase in protein metabolism, the rise was less marked than in the other fevers. Nevertheless, the results are so close that almost all the experiments fall within lines drawn 10 per cent. above and 10 per cent. below the average.

The curve reminds us at once of van't Hoff's law, which for ordinary temperatures may be expressed as follows: "With a rise in temperature of 10° C. the velocity of chemical reactions increases between two and three times." This means an increase of 30 to 60 per cent. for the 3 degrees' rise from 37 to 40 °C. The basal metabolism which represents

Fig. 20



Relation of basal metabolism to temperature in six different fevers. The continuous line shows the average and the dotted lines are drawn to represent metabolism 10 per cent. above and 10 per cent. below the average.

the sum of many chemical reactions within the complex system of the body responds to a rise in temperature in much the same manner as a simple chemical reaction in a test-tube. When the oxidations are increased the tissues need more blood, and we can thus explain part, if not all, of the increased pulse-rate.

Under the heading of protein metabolism in disease we have already discussed the toxic destruction of protein in fever. All the infections, when severe enough to give clinical manifestations known as toxemia, are accompanied by an abnormal breaking down of body protein, with an elimination of nitrogen in the urine which amounts to 20 to 30 even 40 gm. a day. In pulmonary tuberculosis the toxemia and destruction of protein are not nearly so marked as in the more acute fevers. The oxidation of fats and carbohydrates seems to be perfectly normal, carbohydrate being consumed by the tissues whenever it is available. When it is not available the body oxidized its stores of fat and protein.

The old practice of starving fevers was based on the belief that food increased the temperature and toxemia. This was disproved chiefly by the work of Shaffer and Coleman in Bellevue Hospital. They gave typhoid patients 3000 to 5000 calories a day without increasing the temperature. The toxemia was markedly diminished and the clinical results were excellent. Further studies in the Sage calorimeter by Coleman and Du Bois showed that the heat production was not raised by giving typhoid patients large amounts of protein or carbohydrate. McCann and Barr, on the other hand, found a distinct specific dynamic action when protein in large amounts was given in pulmonary tuberculosis. The reason for this apparent discrepancy is quite simple. In typhoid fever the protein metabolism is always high and food simply takes the place of the body protein, causing no rise in heat production. In tuberculosis the protein destruction is moderate and a large protein meal causes stimulation, just as it does in health. In typhoid and other toxic fevers a carbohydrate meal diminishes the protein destruction and this offsets the specific dynamic action of the carbohydrate itself. We may therefore dismiss as a bugaboo the old fear that food increases fever. Even in normal persons the ordinary food causes an increase of only about 6 per cent. in the total metabolism. This is much less than the striking rise due to restlessness in toxic patients. Exact figures are lacking, but we can estimate an increase of 20 to 30 per cent. in a typhoid patient with low muttering delirium.

The groundless prejudice that food is not well absorbed in fever was dispersed many years ago by Prausnitz and a group of Russian investigators. The writer had occasion to analyze the stools of many typhoid patients on the Shaffer-Coleman diet and he found that the absorption was practically normal. The chief objection to a liberal diet in fever is the lack of appetite and the tendency toward vomiting. This can usually be overcome by good nursing with scrupulous care of the nose and mouth. If the food is forced judiciously the appetite returns and the stomach becomes more and more tolerant. Occasionally abdominal distention or diarrhœa becomes troublesome. These symptoms can often be relieved by changing from a carbohydrate to a fat diet or *vice versa*. There is reason to believe that the symptoms are due to changes in the intestinal flora, and this can be altered by changes in the diet.

The most important constituent of the fever diet is *water*. A normal man eliminates about 700 gm of water a day through skin and lungs. A typhoid patient eliminates much more than this because his body is warmer. His kidneys require more water than usual because he has to excrete an abnormal amount of urea.

If we wish to give a typhoid patient an amount of food equal to his heat production we must make the following calculations: His basal metabolism can be estimated from his age, height, and weight. To this we add about 13 per cent. for each degree Centigrade that the temperature is above normal, or 7.2 per cent. for each degree Fahrenheit. We allow perhaps another 10 per cent. if he is toxic with a great destruction of body protein. We add about 10 per cent. for losses in the stools and 10 to 30 per cent. for bodily activity. This gives us the total calories

needed. The best amount of protein is a matter of opinion. I myself try to give 75 to 100 gm. a day (12 to 16 gm. nitrogen). I usually try to give more than half of the calories in the form of carbohydrate, though the patients seem to get along just as well if fat furnishes three-quarters of the non-protein calories. Water must be given either as a constituent of the foods or by itself. Typhoid patients on a diet of, say, 1800 to 2200 calories, just balancing the estimated heat production, will still lose some body protein. If we wish to prevent this we must double the ration. This can usually be done without the slightest harm to the patient. There is still some doubt as to whether or not such diets of 4000 calories are necessary or advisable until the appetite has returned.

In typhoid convalescence the body makes good the losses of body protein and fat. If the diet is liberal all of the fat consumed is stored in the body, and a large proportion of the carbohydrate is transformed into fat. If the patient has been grossly undernourished his metabolism may be below normal in the early stages of convalescence. With growth of new tissue there is a tendency toward increased metabolism, such as we find in youth.

Typhoid fever is the only acute infectious disease in which the metabolism has been thoroughly studied. From the somewhat fragmentary evidence at hand we may assume that the phenomena are almost exactly the same in erysipelas, rheumatic fever and the infections due to pyogenic organisms. In pneumonia the disease is much briefer. There is a local storage of protein and salt in the consolidated lung, with their sudden release during resolution. The basal metabolism is raised just as in other fevers and there is a toxic destruction of protein. Since the whole affair does not often last more than a week, the total loss of body protein and fat is not great. It is in the fevers which last for several weeks that we dread the effects of great destruction of body protein. In the more acute fevers our chief concern is to give enough water and avoid abdominal distention. We should take great care that the patient gets enough carbohydrate food to aid in the complete oxidation of the fat and thus avoid a ketosis. Carbohydrates are believed to diminish the toxic destruction of protein more successfully than isodynamic amounts of fats.

It is not within the scope of the present article to discuss the details of the metabolism in various diseases, since these will be given in other places. There are, however, certain diseases which throw so much light on normal metabolism that they must be mentioned.

Diabetes mellitus furnishes the perfect example of a more or less complete withdrawal of the carbohydrates from the metabolism. As far as I know, every symptom of the disease is due to this one fundamental defect. The loss of glucose in the urine leads to an increased appetite, with loss of weight and strength. Since it requires much water for its excretion it causes polyuria and polydipsia. The fat is incompletely oxidized because there is not enough glucose oxidizing at the same time. This causes the ketosis, with eventual coma. Insulin relieves temporarily all the symptoms if the disease has not advanced too far.

Human diabetes and the experimental pancreatic and phlorhizin diabetes of animals have given us an insight, not only into the origin of

ketosis, but also into the intermediary metabolism of proteins. We know from the D : N ratio that about one-half the protein molecule can be converted into sugar. We also know that fat, except possibly its glycerol radicle, is not converted into sugar or it would be excreted in this form. We cannot be sure that fat is not transformed into some carbohydrate-like substance just before it is oxidized, but if any such action takes place it is neutralized by an equal reaction in the opposite direction.

The basal metabolism in diabetes is not affected until undernutrition becomes apparent and causes the usual diminution in heat production. In some cases of severe diabetes the protein metabolism is greatly increased and the metabolism rises just as it does after a large protein meal. Acidosis may possibly cause an increase of itself.

Obesity of the common type, not due to any ductless gland disease, seems to be a good example of what happens when, through habit or maladjustment of the appetite, we take more calories than we produce. The excess is stored as fat. If, for instance, a man weighing 75 kilograms (165 pounds) takes daily an excess of 11 gm. of butter, he will double his weight in twenty years. That slight excess of calories represents the energy required in walking 1½ miles. It is indeed remarkable that we are not all of us obese in this land of plenty. How can an appetite adjust the intake so that we maintain a constant weight? Why has no one suggested a weight-regulating centre situated in the mid-brain?

Perhaps the most surprising thing connected with common obesity is the unaltered basal metabolism, unaltered in the sense that it is normal per unit of surface area. Each square meter of the skin of a fat man gives off the same amount of heat as each square meter of that of a thin man. Of course, the fat man produces less heat per unit of weight, since a large part of his body is composed of fat, which is inert metabolically. We could explain obesity very nicely if it came as a result of an abnormally low metabolism together with a normal appetite. We could explain persistent and annoying leanness if it came with an abnormally high metabolism. Unfortunately, such theories are not supported by the evidence of the respiratory metabolism except in the distinctly pathological types of hypo- and hyperthyroidism.

There is a peculiarly attractive theory of "luxus consumption" which states that in certain cases of overfeeding the metabolism rises and consumes an abnormal amount of the excess of calories. This is supposed to be distinct from the specific dynamic action of food, which we know does waste some extra calories taken in a heavy meal. The theory of "luxus consumption" would account for the regulation in weight, since it would take care of any excess in the same manner that the spillway of a mill pond takes care of a freshet. Here again experimental evidence is scant, consisting of a few cases of hearty eaters who show a rather high basal metabolism and a large number of people who do not gain weight although they seem to take more calories than can be accounted for by an observation of their daily activities.

The diseases of the *thyroid gland* demonstrate clearly the influence of this organ and its secretion, thyroxin, on the basal metabolism. If the thyroid is absent or functionless, causing complete myxœdema, the basal

metabolism falls about 40 per cent. below the normal. Just why the complete athyreosis should give results so consistently close to −40 per cent. is not clear. With the diminished basal metabolism there naturally results a cold skin, a slow pulse, a diminished appetite, and a tendency to gain weight. The symptoms disappear in a week or two after thyroxin is given intravenously, and Boothby and Plummer have been able to show that the body must contain 12 to 14 mg. of thyroxin in order to hold its basal metabolism at the normal level. This substance is lost or destroyed at the rate of 0.2 to 0.4 mg. daily. Each milligram given intravenously raises the basal metabolic rate about 2.8 per cent. The action of this active principle is rather tardy, much slower than insulin or adrenalin, and it is evident that the thyroid is the slow, steady regulator of the metabolic rate in the tissues of the body.

Hyperthyroidism is accompanied by an increase in basal metabolism which is almost always proportional to the severity of the disease. In extreme cases of exophthalmic goitre the oxidations are increased 75 to 125 per cent.; in moderate cases, say 40 to 75 per cent.; in mild cases 10 to 40 per cent. The symptoms which result from the mere increase in basal metabolism are worth reviewing. In the first place there is an increased appetite and a loss of weight if the appetite does not keep pace with the total metabolism. There is an increased warmth of skin because each square meter of body surface radiates much more heat than normal. This leads to an oppressive sense of warmth on the part of the patient, who does not need as much body clothing or bed clothing as usual. The skin sweats on slight provocation in order to get rid of the extra heat. Since the tissues demand an increased amount of oxygen the heart beats more rapidly, the increase in pulse-rate probably being roughly in proportion to the increased metabolism, since it is due almost entirely to this cause. The observant clinician, noting the extent of the symptoms, can often form a close estimate of the metabolic rate.

The relationship between certain symptoms and the metabolism is well illustrated by a case which came under the writer's observation. A woman who had been married about ten years developed a sense of fatigue with rapid pulse even when resting quietly in bed. There was no exophthalmos, no tremor, no enlargement of the thyroid. She was questioned carefully regarding the number of blankets she used at night. Since the husband slept in the same room he was used as a normal control, just as in a metabolism experiment. The history made the diagnosis. For nine years the wife had always needed one or two more blankets than the husband. With the onset of fatigue and rapid pulse she noticed that she could get along with the same number of blankets. As the symptoms grew worse she was able to keep quite warm with one blanket, while the normal control needed two or three. A respiration test showed that her metabolism was 35 per cent. above the normal. Fortunately the early recognition of the hyperthyroidism made it possible to insist on a rest cure which resulted in a complete recovery. At the end of three months she needed more blankets than the husband and the pulse-rate taken in the early morning was perfectly normal.

Experiments made after the subcutaneous administration of *epinephrine* show a sudden increase in metabolism. The adrenals seem to act as

emergency regulators of metabolism. The effects of various pituitary extracts are less marked, and it is doubtful if this organ has a direct control over the basal rate. Some cases of acromegaly show an increased metabolism, but this seems to be due to a synchronous involvement of the thyroid gland. The lowered metabolism in obesity of pituitary origin is assumed to be due to a diminished thyroid function. Castration causes a moderate fall in the metabolism in many cases, and this is also assumed to result from a change in the thyroid gland.

The relationship of *mental activity* to the metabolism has not yet been closely established. It would seem as if a few brain cells could do a great deal of thinking without using up enough oxygen to raise appreciably the total consumption in the body. Some observers have noted a small increase in metabolism during mental activity, possibly referable to a change in muscular tone or to an indirect influence of the nervous system. The most striking results were obtained by Grafe, who hypnotized a number of normal men and then suggested to them all sorts of terrible calamities. In two-thirds of the cases the metabolsm rose 5 to 25 per cent., in the remainder there was no change. The laity believe that mental effort uses up large amounts of food, but this is only a general impression as yet unsupported by proof. It is well known that mental anxiety leads to a loss of weight, but this may be due to a loss of appetite.

As a general review of the subject of basal metabolism in disease we can recommend nothing better than a study of the following tables taken from the work of Boothby at the Mayo Clinic.

TABLE 18.—COMPARISON OF THE BASAL METABOLIC RATE IN 6197 PATIENTS WITH THYROID DISORDERS. (BOOTHBY.)

Diagnosis.	Cases.	Percentage range.								
		Above + 20.	+ 20 to + 16.	+ 20 to + 11.	+ 15 to + 11.	Normal + 10 to − 10.	− 11 to − 15.	− 11 to − 20.	− 16 to − 20.	Below − 20.
		%	%	%	%	%	%	%	%	%
Exophthalmic goitre	2569	93	..	5	..	2				
Recurrent exophthalmic goitre	320	90	6	..	2	2				
Adenoma with hyperthyroidism	1425	68	..	32						
Recurrent adenoma with hyperthyroidism	46	57	17	..	26					
Adenoma without hyperthyroidism	1111	..	..	..	..	100				
Recurrent adenoma without hyperthyroidism	62	..	..	..	..	90	8	..	2	
Colloid goitre	328	..	3	..	10	79	6	..	1	1
Myxœdema	102	..	..	..	..	..	..	20	..	80
Postoperative myxœdema	41	..	..	..	..	..	..	46	..	54
Questionable hypothyroidism	86	..	..	..	..	9	..	61	..	30
Cretinism	28	..	..	..	..	21	..	32	..	47
Thyroiditis	34	32	..	12	..	35	..	12	..	9
Malignant thyroid	45	22	..	9	..	67	..	..	..	2
Total	6197									

TABLE 19.—THE BASAL METABOLIC RATE IN CONDITIONS NOT DUE TO THYROID DISORDERS. (BOOTHBY.)

Diagnosis.	Cases.	Percentage range.							
		Below −20.	−20 to −16.	−15 to −11.	−10 to +10.	+11 to +15.	+16 to +20.	Above +20.	−15 to +15.
		%	%	%	%	%	%	%	%
Normals	127	..	..	3.2	92.1	4.0	0.7	..	99.3
Migraine	31	..	..	6.4	93.6	..	..	..	100.0
Chronic nervous exhaustion	267	..	1.2	2.3	87.3	8.6	0.7	..	98.2
Neurasthenia	384	..	0.3	3.6	84.3	9.4	1.4	1.0	97.3
Obesity	94	1.1	3.2	6.4	80.7	7.5	1.1	..	94.6
Asthenia	36	..	2.7	11.2	77.8	8.3	..	..	97.2
Essential hypertension	170	..	..	0.6	73.0	15.8	7.2	3.4	89.4
Cardiac neurosis	99	..	1.0	2.0	83.9	10.1	1.0	2.0	96.0
Heart-block	10	..	..	..	80.0	10.0	..	10.0	90.0
Endocarditis	56	..	..	1.8	80.4	5.4	1.8	10.6	87.6
Myocarditis	55	1.8	..	3.6	81.9	10.9	..	1.8	96.4
Pericarditis	4	..	..	..	100.0	..	..	..	100.0
Congenital heart	5	..	..	..	80.0	20.0	..	..	100.0
Renal	127	4.0	1.6	3.2	72.4	12.6	4.0	2.4	88.2
Hodgkin's disease	1	..	..	..	..	..	..	100.0	
Mental	34	3.0	3.0	8.9	61.7	17.6	2.9	2.9	88.2
Epilepsy	22	9.1	4.6	9.1	77.3	..	..	..	86.4
Gastro-intestinal	98	1.0	1.0	3.1	85.7	4.1	5.1	..	92.9
Gynecological	96	1.0	2.1	6.3	81.3	4.1	5.2	..	91.7
Malignancy	10	..	5.0	..	55.0	10.0	10.0	20.0	65.0
Dermatological	43	2.3	..	14.0	79.1	4.6	..	..	97.7
Pregnancy	30	..	..	..	70.0	10.0	10.0	10.0	80.0
Encephalitis	10	..	..	10.0	70.0	..	..	20.0	80.0
Dysphagia	65	16.9	6.2	10.7	63.1	3.1	..	..	76.9
Acromegaly	30	3.3	..	3.3	43.4	13.3	10.0	26.7	60.0
Hypopituitarism	58	12.1	25.9	15.5	34.5	5.2	3.4	3.4	55.2
Paget's disease	6	..	..	..	66.7	16.7	..	16.6	83.4
Addison's disease	13	15.4	..	7.7	69.2	..	..	7.7	76.9
Polycythemia	2	..	..	..	50.0	..	..	50.0	50.0
Secondary anemia	30	..	3.3	..	80.0	13.4	..	3.3	93.4
Anemia, splenic and pernicious	19	..	..	15.9	63.0	10.5	..	10.6	89.4
Leukemia, lymphatic and myelogenous	16	..	..	..	6.3	6.3	..	87.5	12.6
Questionable ductless glands	24	8.3	8.3	16.6	58.4	..	..	8.4	75.0
Sclerosis of central nervous system; tabes	20	..	..	..	90.0	10.0	..	..	100.0
Diabetes	68	17.7	10.3	7.3	52.9	..	5.9	5.9	60.2
Arthritis	69	2.8	2.8	5.7	75.3	11.6	1.4	..	92.6
Misc., not thyroid	178	..	2.7	5.6	77.1	8.4	4.0	2.2	91.1
Total	2417	2.1	2.2	4.6	77.1	8.3	2.6	3.1	90.0

In them the findings are referred to the Sage standards of normal metabolism. It will be noted that the large majority of cases fall within the normal limits of − 10 to +10 per cent. except in thyroid disease, pituitary disease, leukemia, fever, and dysphagia with undernutrition.

Food as it Affects Respiration.—McCann has called our attention to the manner in which food affects the respiration, particularly in pulmonary tuberculosis. McCann and Barr demonstrated that a large protein meal in tuberculosis has about the same specific dynamic action as in health. They found that 70 gm. of protein with 28 gm. of fat increased the metabolism about 21 per cent. This caused a proportionate increase in respiration. One hundred grams of sugar does not cause such a rise in oxygen consumption, but on account of its high respiratory quotient causes a great increase in carbon dioxide elimination. Since the carbon dioxide is the chief respiratory stimulant, the respiration increases out of proportion to the metabolism. McCann found an increase of 70 per cent. in the pulmonary ventilation after 100 gm. of sugar. Fat, with its low specific dynamic action and low respiratory quotient, causes but little rise in the ventilation of the lungs. If, therefore, we wish to diminish the work of the lungs we must avoid overfeeding with protein and carbohydrate.

Practical Applications.—Under ordinary conditions we can allow our patients to take the diets that have been handed down by previous generations of clinicians and hospital dietitians. These have the sanction of custom; patients and their relatives accept them with confidence. With ambulatory patients there is usually no need of making marked changes in the diet unless there have been gross errors. It does not seem right to change a person's food simply in order to impress him with the fact that his doctor is an expert in dietetics.

If we are going to construct a diet for a certain patient we must consider many factors. They may be roughly classified as follows:

FACTORS TO BE CONSIDERED IN PLANNING A DIET.

The Disease:
- Its effect on the metabolism.
- Its effect on the gastro-intestinal tract.
- Its effect on the circulation and kidneys.

The Patient:
- His purse and place of eating.
- His age, size, and basal metabolism.
- His activity and total metabolism.
- His state of nutrition.
- His appetite.
- His food idiosyncrasies and personal likes and dislikes.

The Physician:
- His personal likes and dislikes.
- His leanings toward certain theories.
- His reactions against certain fads.
- His desire to change the patient's metabolism.
- His desire to affect the stomach or intestines.
- His desire to spare the kidneys.

The Food:
- Good quality and good cooking.
- Attractive appearance and proper temperature.
- Total calories adjusted to needs.

The Food:

Protein in the specified amount.
Enough good quality protein (meat, milk, eggs, etc.) to furnish the required amino-acids.
Carbohydrate enough to prevent ketosis and more, if possible.
Fat to supply the remaining calories.
Plenty of water.
Fruits and green vegetables for bulk, vitamines, and salts.
Flavors and tea, coffee, and other foolish and harmful tid-bits which make meals worth eating.
A cheerful spirit at meal time which makes life worth living.

TABLE 20.—TABLE OF FOOD VALUES, WEIGHTS AND MEASURES.

Average Chemical Composition of American Foods.[1]

Food material.	Water. Per cent.	Protein, Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
ANIMAL FOOD.					
A. BEEF.					
Fresh:					
Chuck, including shoulder	65.0	19.2	15.4	...	222
Loin	61.3	19.0	19.1	...	255
Sirloin butt, as purchased	62.5	19.7	17.7	...	246
Porterhouse steak	60.0	21.9	20.4	...	280
Ribs	57.0	17.8	24.6	...	302
Round	67.8	20.9	18.6	...	184
Beef Organs:					
Brain	80.6	8.8	9.3	...	122
Kidney	76.7	16.6	4.8	0.4	115
Beef liver	71.2	20.4	4.5	1.7	133
Sweetbreads, as purchased	70.9	16.8	12.1	...	181
Tongue	70.8	18.9	9.2	...	163
Cooked:					
Roast, as purchased	48.2	22.3	28.6	...	357
Round steak, fat removed, as purchased	63.0	27.6	7.7	...	185
Loin steak:					
Tenderloin, broiled	54.8	23.5	20.4	...	287
Canned:					
Boiled beef, as purchased	51.8	25.5	22.5	...	314
Corned beef	51.8	26.3	18.7	...	282
Roast beef, as purchased	58.9	25.9	14.8	...	243
B. VEAL.					
Fresh:					
Breast	68.2	20.3	11.0	...	185
Leg	71.7	20.7	6.7	...	146
Loin	69.5	19.9	10.0	...	174
Rib	69.8	20.2	9.4	...	170
Shoulder and flank, medium fat	65.2	19.7	14.4	...	215
Kidney, as purchased	75.8	16.9	6.4	...	129
C. LAMB.					
Fresh:					
Breast or chuck	56.2	19.1	23.6	...	298
Leg, hind	58.6	18.6	22.6	...	287
Shoulder	51.8	18.1	29.7	...	351
Forequarter	55.1	18.3	25.8	...	315
Hindquarter	60.9	19.6	19.1	...	258

[1] From Atwater and Bryant (Abstract, United States Department of Agriculture, Bulletin No. 28, 1906.) Carter, Howe and Mason, *Nutrition and Clinical Dietetics*, Lea & Febiger, 1923.

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
ANIMAL FOOD.					
C. Lamb.					
Cooked:					
Chops, broiled	47.6	21.7	29.9	...	367
Leg, roast	67.1	19.7	12.7	...	198
D. Mutton.					
Fresh:					
Chuck, lean	64.7	17.8	16.3	...	225
Leg, hind	63.2	18.7	17.5	...	239
Shoulder	60.2	17.5	21.8	...	274
Forequarter	52.9	15.6	30.9	...	352
Cooked:					
Mutton, leg, roast	50.9	25.0	22.6	...	313
E. Pork.					
Fresh:					
Ham	50.1	15.7	33.4	...	375
Pickled, salted and smoked:					
Ham, smoked, boiled, as purchased	51.3	20.2	22.4	...	291
fried, as purchased	36.6	22.2	33.2	...	400
Bacon, smoked	20.2	10.5	64.8	...	646
F. Sausage. (As purchased.)					
Bologna	55.2	18.2	19.7	...	258
Frankfurt	57.2	19.6	18.6	1.1	258
Pork	39.8	13.0	44.2	1.1	468
Sausage meat	46.2	17.4	32.5	...	374
G. Poultry.					
Fresh:					
Chicken, broiler	69.7	20.7	8.3	...	196
young, dark meat	70.1	20.8	8.2	...	187
light meat	70.3	21.9	7.4	...	184
Duck, breast	73.9	22.3	2.3	...	151
Guinea-hen meat, not including giblets	68.9	23.4	6.5	...	191
Pheasant meat, not including giblets	70.0	24.7	4.6	...	180
Pigeon meat, not including giblets	63.2	22.9	12.1	...	243
Quail meat, not including giblets	66.3	25.4	7.0	...	208
Squab meat, not including giblets	56.6	18.5	23.8	...	324
Turkey, dark meat	57.0	21.4	20.6	...	316
cooked	53.7	39.2	4.3	...	265
light meat	63.9	25.7	9.4	...	235
cooked	58.5	34.6	4.9	...	240
Preserved Poultry Meat:					
Potted turkey	56.0	17.2	22.0	...	306
chicken	56.1	19.4	20.3	...	306
Canned chicken soup	87.1	2.9	3.3	5.1	66
gumbo soup	91.0	2.4	0.2	4.8	35
boned chicken	57.6	27.7	12.8	...	274
H. Fish.					
Fresh:					
Cod, whole	82.6	16.5	0.4	1.2	103
Bass, black, whole	76.7	20.6	1.7	1.2	103
sea, whole	79.3	19.8	0.5	1.4	86
striped, whole	77.7	18.6	2.8	1.2	102
Blackfish, whole	70.1	18.7	1.2	1.1	80

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
ANIMAL FOOD.					
H. Fish.—*Continued.*					
Fresh:					
Bluefish, entrails removed	78.5	19.4	1.2	1.3	90
Butterfish, whole	70.0	18.0	11.0	1.2	176
Eels, salt water	71.6	18.6	9.1	1.0	161
Haddock, entrails removed	81.7	17.2	0.3	1.2	74
Halibut, steak or sections	75.4	18.6	5.2	1.0	125
Herring, whole	72.5	19.5	7.1	1.5	146
Mackerel, whole	73.4	18.7	7.1	1.2	142
Perch, white, whole	75.7	19.3	4.0	1.2	117
as purchased	28.4	7.3	1.5	0.4	44
yellow, whole	79.3	18.7	0.8	1.2	84
Pickerel, pike, whole	79.8	18.7	0.5	1.1	81
Pike, gray, whole	80.8	17.9	0.8	1.1	80
Pompano, whole	72.8	18.8	7.5	1.0	147
Porgy (scup), whole	75.0	18.6	5.1	1.4	123
Salmon, whole	64.6	22.0	12.8	1.4	209
Shad, whole	70.6	18.8	9.5	1.3	165
roe, as purchased	71.2	20.9	3.8	1.5	133
Smelt, whole	79.2	17.6	1.8	1.7	89
Spanish mackerel, whole	68.1	21.5	9.4	1.5	175
Trout, brook, whole	77.8	19.2	2.1	1.2	98
Preserved and canned:					
Cod, salt	53.5	25.4	0.3	...	90
Herring, smoked	34.6	36.9	15.8	...	299
Mackerel, salt, dressed	43.4	17.3	26.4	...	316
Salmon, canned	63.5	21.8	12.1	...	201
Sardines, canned	52.3	23.0	19.7	...	278
Shellfish, etc., Fresh:					
Clams, round, removed from shell, as purchased	80.8	10.6	1.1	5.2	75
Oysters, solids, as purchased	88.3	6.0	1.3	3.3	51
Scallops, as purchased	80.3	14.8	0.1	3.4	76
I. Eggs.					
Hens', uncooked	73.7	13.4	10.5	...	159
boiled	73.2	13.2	12.0	...	169
whites	86.2	12.3	0.2	...	55
yolks	49.5	15.7	33.3	...	376
Egg, boiled, 1 egg (50 gm.)	36.6	6.6	6.0	...	169
			Total, 1 egg	...	83
J. Dairy Products, etc. (As purchased.)					
Butter	11.0	1.0	85.0	...	795
Buttermilk	91.0	3.0	0.5	4.8	36
Cheese, American, pale	31.6	28.8	35.9	0.3	453
red	28.6	29.6	38.3	...	477
California flat	34.0	24.3	33.4	4.5	429
Cheddar	27.4	27.7	36.8	4.1	473
Cheshire	37.1	26.9	30.7	0.9	399
Cottage	72.0	20.9	1.0	4.3	112
Dutch	35.2	37.1	17.7	...	316
Full cream	34.2	25.9	33.7	2.4	430
Limburger	42.1	23.0	29.4	0.4	369
Neufchatel	50.0	18.7	27.4	1.5	337
Roquefort	29.3	22.6	29.5	1.8	375
Swiss	31.4	27.6	24.9	1.3	443
Cream	74.0	2.5	18.5	4.5	201
Koumyss	89.3	2.8	2.1	5.4	53

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
ANIMAL FOOD.					
J. Dairy Products, etc.—*Continued.*					
Milk, condensed, sweetened	26.9	8.8	8.3	54.1	335
unsweetened (evaporated cream)	68.2	9.6	9.3	11.2	172
skimmed	90.5	3.4	0.3	5.1	37
whole	87.0	3.3	4.0	5.0	72
whey	93.0	1.0	0.3	5.0	28
K. Miscellaneous. (As purchased.)					
Beef-juice	93.0	4.9	0.6	...	25
Calf's-foot jelly	77.6	4.3	....	17.4	89
Oleomargarine	9.5	1.2	83.0	...	777
VEGETABLE FOOD.					
A. Flour, Meals, etc.					
Barley meal and flour	11.9	10.5	2.2	72.8	362
Buckwheat flour	13.6	6.4	1.2	77.9	357
Cornmeal, granular	12.5	9.2	1.9	75.4	365
Corn Preparations:					
Cerealine	10.3	9.6	1.1	78.3	370
Hominy	11.8	8.3	0.6	79.0	364
cooked	79.3	2.2	0.2	17.8	84
Oatmeal	7.3	16.1	7.2	67.5	410
boiled	84.5	2.8	0.5	11.5	63
gruel	91.6	1.2	0.4	6.3	34
water	96.0	0.7	0.1	2.9	15
Rolled oats	7.7	16.7	7.3	66.2	408
Rice	12.3	8.0	0.3	79.0	359
boiled	72.5	2.8	0.1	24.4	112
flaked	9.5	7.9	0.4	81.9	371
flour	8.5	8.6	6.1	68.0	370
Rye flour	12.9	6.8	0.9	78.7	359
meal	11.4	13.6	2.0	71.5	367
Wheat, entire	11.4	13.8	1.9	71.9	369
gluten	12.0	14.2	1.8	71.1	367
Graham	11.3	13.3	2.2	71.4	368
Prepared (self-raising)	10.8	10.2	1.2	73.0	353
Wheat Preparations:					
Cracked and crushed	10.1	11.1	1.7	75.5	371
Farina	10.9	11.0	1.4	76.3	371
Flaked	8.7	13.4	1.4	74.3	373
Gems	10.4	10.5	2.0	76.0	374
Glutens	8.9	13.6	1.7	74.6	378
Macaroni	10.3	13.4	0.9	74.1	367
cooked	78.4	3.0	1.5	15.8	91
Noodles	10.7	11.7	1.0	75.6	367
Shredded	8.1	10.5	1.4	77.9	375
Spaghetti	10.6	12.1	0.4	76.3	366
Vermicelli	11.0	10.9	2.0	72.0	358
B. Bread, Crackers, Pastry, etc. (As purchased.)					
Bread:					
Brown	43.6	5.4	1.8	47.1	231
Corn (johnny cake)	38.9	7.9	4.7	46.3	266
Rye	35.7	9.0	0.6	53.2	260
Wheat:					
Buns	29.0	6.3	6.5	57.3	321
Cinnamon	23.6	9.4	7.2	59.1	347
Currant	27.5	6.7	7.6	57.6	334

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
VEGETABLE FOOD.					
B. Bread, Crackers, Pastry, etc.—*Continued.*					
Bread, Wheat: Hot cross	36.7	7.9	4.8	49.7	281
Graham	35.7	8.9	1.8	52.1	267
Biscuit, home-made	32.9	8.7	2.6	55.3	287
soda	22.9	9.3	13.7	52.6	381
Rolls, French	32.0	8.5	2.5	55.7	287
Vienna	31.7	8.5	2.2	56.5	287
White, biscuit	35.2	8.0	1.4	54.3	269
home-made	35.0	9.1	1.6	53.3	270
all analyses	35.3	9.2	1.3	53.1	268
Whole wheat	38.4	9.7	0.9	49.7	251
Zwieback	5.8	9.8	9.9	73.5	434
Crackers:					
Soda	5.9	9.8	9.1	73.1	424
Boston (split)	7.5	11.0	8.5	71.1	416
Egg	5.8	12.6	14.0	66.6	454
Graham	5.4	10.0	9.4	73.8	429
Oatmeal	6.3	11.8	11.1	69.0	434
Oyster	4.8	11.3	10.5	70.5	433
Pretzels	9.6	9.7	3.9	72.8	375
Saltines	5.6	10.6	12.7	68.5	442
Water	6.4	11.7	5.0	75.7	405
All analyses	6.8	10.7	8.8	71.9	420
Cake:					
Bakers'	31.4	6.3	4.6	59.9	302
Chocolate layer	20.5	6.2	8.1	64.1	364
Drop	16.6	7.6	14.7	60.3	316
Frosted	18.2	5.9	9.0	64.8	374
Fruit	17.3	5.9	10.9	64.1	388
Gingerbread	18.8	5.8	9.0	63.5	368
Sponge	15.3	6.3	10.7	65.9	396
Cookies, Cakes, etc.:					
Molasses cookies	6.2	7.2	8.7	75.7	421
Sugar cookies	8.3	7.0	10.2	73.2	423
Ginger snaps	6.3	6.5	8.6	76.0	418
Lady fingers	15.0	8.8	5.0	70.6	371
Macaroons	12.3	6.5	15.2	65.2	435
Doughnuts	18.3	6.7	21.0	53.1	441
Pie:					
Apple	42.5	3.1	9.8	42.8	280
Cream	32.0	4.4	11.4	51.2	334
Custard	62.4	4.2	6.3	26.1	183
Lemon	47.4	3.6	10.1	37.4	262
Mince	41.3	5.8	12.3	38.1	294
Squash	64.2	4.4	8.4	21.7	185
Puddings:					
Rice custard	59.4	4.0	4.6	31.4	182
Indian meal	60.7	5.5	4.8	27.5	180
Tapioca	64.5	3.3	3.2	28.2	159
Tapioca with apple	70.1	0.3	0.1	29.3	122
Ice-cream	66.9	5.2	10.1	17.7	189

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
VEGETABLE FOOD.					
C. Sugars, Starches, etc. (As purchased.)					
Candy	....	....	....	96.0	391
Honey	18.2	0.4	....	81.2	335
Molasses, cane	25.1	2.4	....	69.3	284
Starch, tapioca	11.4	0.4	0.1	88.0	364
Sugar, coffee or brown	....	....	....	95.0	389
granulated	....	....	....	100.0	410
maple	....	....	....	82.8	339
powdered	....	....	....	100.0	410
D. Vegetables.					
Artichokes, as purchased	79.5	2.6	0.2	16.7	80
Asparagus, cooked, as purchased	91.1	2.1	3.3	2.2	48
Beans, butter, green	58.9	9.4	0.6	29.1	163
String beans, cooked	95.3	0.8	1.1	1.9	21
fresh, as purchased	83.0	2.1	0.3	6.9	40
Beets, cooked	88.6	2.3	0.1	7.4	41
Cabbage	91.5	1.6	0.3	5.6	32
Carrots, fresh	88.2	1.1	0.4	9.3	46
Cauliflower, as purchased	92.3	1.8	0.5	4.7	31
Celery	94.5	1.1	0.1	3.3	19
Corn, green	75.4	3.1	1.1	19.7	104
Cucumbers	95.4	0.8	0.2	3.1	18
Eggplant	92.9	1.2	0.3	5.1	29
Greens, beet, cooked, as purchased	89.5	2.2	3.4	3.2	54
Lentils, dried, as purchased	8.4	25.7	1.0	59.2	357
Lettuce	94.7	1.2	0.3	2.9	20
Mushrooms, as purchased	88.1	3.5	0.4	6.8	46
Okra	90.2	1.6	0.2	7.4	39
Onions, fresh	87.6	1.6	0.3	9.9	49
prepared, as purchased	91.2	1.2	1.8	4.9	42
Parsnips	83.0	1.6	0.5	13.5	66
Peas, dried, as purchased	9.5	24.6	1.0	62.0	365
green	74.6	7.0	0.5	16.9	102
cooked, as purchased	73.8	6.7	3.4	14.6	119
Potatoes, raw or fresh cooked	78.3	2.2	0.1	18.4	85
boiled, as purchased	75.5	2.5	0.1	20.9	97
cooked chips, as purchased	2.2	6.8	39.8	46.7	589
mashed and creamed, as purchased	75.1	2.6	3.0	17.8	111
sweet, raw or fresh	69.0	1.8	0.7	27.4	126
cooked and prepared, as purchased	51.9	3.0	2.1	42.1	204
Pumpkins	93.1	1.0	0.1	5.2	26
Radishes	91.8	1.3	0.1	5.8	30
Rhubarb	94.4	0.6	0.7	3.6	23
Sauerkraut, as purchased	88.8	1.7	0.5	3.8	28
Spinach, fresh, as purchased	92.3	2.1	0.3	3.2	24
cooked, as purchased	89.8	2.1	4.1	2.6	57
Squash	88.3	1.4	0.5	9.0	47
Tomatoes, fresh, as purchased	94.3	0.9	0.4	3.9	23
Turnips	89.6	1.3	0.2	8.1	41

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
VEGETABLE FOOD.					
D. VEGETABLES.—*Continued.*					
Canned as Purchased.					
Asparagus	94.4	1.5	0.1	2.8	19
Beans, baked	68.9	6.9	2.5	19.6	132
string	93.7	1.1	0.1	3.8	21
lima	79.5	4.0	0.3	14.6	79
red kidney	72.7	7.0	0.2	18.5	106
Brussels sprouts	93.7	1.5	0.1	3.4	21
Corn, green	76.1	2.8	1.2	19.0	103
Okra	94.4	0.7	0.1	3.6	19
Peas, green	85.3	3.6	0.2	9.8	56
Pumpkins	91.6	0.8	0.2	6.7	33
Squash	87.6	0.9	0.5	10.5	52
Succotash	75.9	3.6	1.0	18.6	103
Tomatoes	94.0	1.2	0.2	4.0	23
F. FRUITS, BERRIES.					
Apples:					
Edible portion	84.6	0.4	0.5	14.2	64
As purchased (refuse, 25.0)	63.3	0.3	0.3	10.8	49
Apricots	85.0	1.1	....	13.4	59
Bananas:					
Edible portion	75.3	1.3	0.6	22.0	101
As purchased (refuse, 35.0)	48.9	0.8	0.4	14.3	66
Blackberries, as purchased	86.3	1.3	1.0	10.9	15
Cherries, as purchased	76.8	0.9	0.8	15.9	76
Cranberries, as purchased	88.9	0.4	0.6	9.9	47
Currants, as purchased	85.0	1.5	....	12.8	58
Figs, fresh, as purchased	79.1	1.5	....	18.8	84
Grapes, as purchased	58.0	1.0	1.2	14.4	74
Huckleberries	81.9	0.6	0.6	16.6	76
Lemons:					
Edible portion	89.3	1.0	0.7	8.5	45
As purchased (refuse, 30.0)	62.5	0.7	0.5	5.9	32
Muskmelons:					
Edible portion	89.5	0.6	....	9.3	41
As purchased (refuse, 50.0)	44.8	0.3	....	4.6	20
Nectarines	82.9	0.6	....	15.9	67
Oranges:					
Edible portion	86.9	0.8	0.2	11.6	53
As purchased (refuse, 27.0)	63.4	0.6	0.1	8.5	37
Peaches:					
Edible portion	69.4	0.7	0.1	9.4	42
As purchased (refuse, 18.0)	73.3	0.5	0.1	7.7	34
Pears:					
Edible portion	64.4	0.6	0.5	14.1	65
As purchased (refuse, 10.0)	76.0	0.5	0.4	12.7	57
Pineapple	89.3	0.4	0.3	9.7	44
Prunes	79.6	0.9	....	18.9	81
Raspberries, as purchased	85.8	1.0	....	12.6	56
Strawberries	90.4	1.0	0.6	7.4	40
Watermelons:					
Edible portion	92.4	0.4	0.2	6.7	31
As purchased (refuse, 59.4)	37.5	0.2	0.1	2.7	13
Dried.					
Apples, as purchased	28.1	1.6	2.2	66.1	298
Apricots, as purchased	29.4	4.7	1.0	62.5	284
Citron, as purchased	19.0	0.5	1.5	78.1	336

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
VEGETABLE FOOD.					
F. Fruits, Berries, etc.—*Continued.*					
Currants, as purchased	17.2	2.4	1.7	74.2	330
Dates	15.4	2.1	2.8	78.4	336
Figs, as purchased	18.8	4.3	0.3	74.2	325
Pears	16.5	2.8	5.4	72.9	360
Prunes	22.3	2.1	....	73.3	309
Raisins	14.6	2.6	3.3	76.1	354
Canned and Jellies.					
Preserves, etc., as purchased:					
Apples, crab	42.4	0.3	2.4	54.4	247
sauce	61.1	0.2	0.8	37.2	161
Apricots	81.4	0.9	....	17.3	75
Blackberries	40.0	0.8	2.1	56.4	254
Blueberries	85.6	0.6	0.6	12.8	61
Cherries	77.2	1.1	0.1	21.1	91
Figs, stewed	56.5	1.2	0.3	40.9	173
Marmalade (orange peel)	14.5	0.6	0.1	84.5	349
Peaches	88.1	0.7	0.1	10.8	49
Pears	81.1	0.3	0.3	18.0	78
Strawberries, stewed	74.8	0.7	....	24.0	101
Prune sauce	76.6	0.5	0.1	22.3	95
G. Nuts.					
Almonds	4.8	21.0	54.9	17.3	668
Beechnut	4.0	21.9	57.4	13.2	678
Brazil nuts (Bertholletia' excelsa), edible portion	5.3	17.0	66.8	7.0	720
Butternuts:					
Juglans cinerea	4.4	27.9	61.2	3.5	698
Chestnuts:					
Edible portion	45.0	6.2	5.4	42.1	246
As purchased (refuse, 16.0)	37.8	5.2	4.5	35.4	208
Cocoanuts	14.1	5.7	50.6	27.9	608
Cocoanut, prepared, as purchased	3.5	6.3	57.4	31.5	689
Filberts	3.7	15.6	65.3	13.0	725
Hickory nuts	3.7	15.4	67.4	11.4	737
Lichi nuts	17.9	2.9	0.2	77.5	332
Peanuts:					
Edible portion	9.2	25.8	38.6	24.4	564
As purchased (refuse, 24.5)	6.9	19.5	29.1	18.5	427
Peanut butter, as purchased	2.1	29.3	46.5	17.1	623
Walnuts, California	2.5	18.4	64.4	13.0	728
H. Miscellaneous.					
Chocolate	5.9	12.9	48.7	30.3	631
Cocoa	4.6	21.6	28.9	37.7	511
UNCLASSIFIED FOOD MATERIALS.					
Animal and Vegetable.					
A. Soups.					
Home-made (*as purchased*).					
Beef	92.9	4.4	0.4	1.1	26
Bean	84.3	3.2	1.4	9.4	65
Chicken	84.3	10.5	0.8	2.4	61
Chowder, clam	88.7	1.8	0.8	6.7	43
Meat stew	84.5	4.6	4.3	5.5	81

Food material.	Water. Per cent.	Protein. Per cent.	Fat. Per cent.	Carbohydrates. Per cent.	Calories. Per 100 gm.
UNCLASSIFIED FOOD MATERIAL.					
A. Soups.—*Continued. Canned as Purchased.*					
Asparagus, cream of	87.4	2.5	3.2	5.5	63
Bouillon	96.6	2.2	0.1	0.2	11
Celery, cream of	88.6	2.1	2.8	5.0	55
Chicken	93.8	3.6	0.1	1.5	22
gumbo	89.2	3.8	0.9	4.7	43
Consommé	96.0	2.5	....	0.4	12
Corn, cream of	86.8	2.5	1.9	7.8	59
Julienne	95.9	2.7	....	0.5	13
Mock turtle	89.8	5.2	0.9	2.8	41
Mulligatawny	89.3	3.7	0.1	5.7	40
Oxtail	88.8	4.0	1.3	4.3	46
Pea	86.9	3.6	0.7	7.6	52
cream of green	87.7	2.6	2.7	5.7	60
Tomato	90.0	1.8	1.1	5.6	41
Turtle, green	86.6	6.1	1.9	3.9	58
Vegetable	95.7	2.9	....	0.5	14
B. Miscellaneous.					
Hash	80.3	6.0	1.9	9.4	80
Mincemeat, commercial	27.7	6.7	1.4	60.2	288
home-made	54.4	4.8	6.7	32.1	214
Salad, ham	69.4	15.4	7.6	5.6	157
Sandwich, egg	41.4	9.6	12.7	34.5	299
chicken	48.5	12.3	5.4	32.1	232

Table of Measures and Weights.

4 saltspoonfuls	=	1 teaspoonful
3 teaspoonfuls	=	1 tablespoonful
4 tablespoonfuls	=	¼ cup or ½ gill
16 tablespoonfuls (dry)	=	1 cup
16 tablespoonfuls (wet)	=	1 cup
2 gills	=	1 cup (8 oz. or 250 cc)
2 cups	=	1 pint (16 oz. or 500 cc)
2 pints	=	1 quart (32 oz. or 1000 cc)
4 quarts	=	1 gallon (128 oz. or 4000 cc)
2 tablespoonfuls butter	=	1 ounce (30 gm.)
4 tablespoonfuls flour	=	1 ounce (30 gm.)
2 tablespoonfuls granul'd sugar	=	1 ounce (30 gm.)
2 tablespoonfuls liquid	=	1 ounce (30 cc)
5 tablespoonfuls liquid	=	1 wineglassful
Apothecaries' Measures.		
60 minims (M)	=	1 fluidram (4 cc)
8 fluidrams	=	1 fluidounce (30 cc)
16 fluidounces	=	1 pint (500 cc)
2 pints	=	1 quart (1000 cc)
4 quarts	=	1 gallon (4000 cc)
Apothecaries' Weights.		
20 grains	=	1 scruple (1⅓ gm.)
3 scruples	=	1 dram (4 gm.)
8 drams (480 grains)	=	1 ounce (30 gm.)
12 ounces	=	1 pound (360 gm.)
Approximate Measures.		
1 teaspoonful	=	about 1 fluidram (4 cc)
1 dessertspoonful	=	2 fluidrams (8 cc)
1 tablespoonful	=	4 fluidrams (15 cc)
1 wineglassful	=	2 ounces (60 cc)

CHAPTER II

DIABETES MELLITUS AND INSIPIDUS

By THOMAS B. FUTCHER, M.D.

DIABETES MELLITUS

Definition.—A disorder primarily of carbohydrate, and secondarily of fat and protein metabolism, due to the failure of the system to burn sugar, and dependent upon a deficiency or absence of the internal secretion of the pancreas, resulting from functional or organic disease of the islands of Langerhans. The isolation of insulin by Banting has undoubtedly established the unity of the disease.

Incidence.—A study of the *incidence* of the disease would seem to indicate that it was on the increase in the United States. The United States census for 1850 gave 0.9; for 1860, 1.2; for 1870, 2.1; for 1880, 2.8; for 1890, 5.5; for 1900, 9.3; for 1910, 14.9; and for 1920, 16.1 deaths from diabetes per 100,000 population in the registration area. In the census year 1920 there were 14,062 deaths from the disease in the United States. They constituted 1.22 per cent. of 1,142,558 total deaths for this year. Joslin, Haven Emerson and Larrimore have demonstrated the steady increase in the mortality from the disease in Boston and New York respectively. There has been the same progressive increase in the incidence of the disease in Baltimore. Joslin estimates that there are 2,000,000 diabetics in the United States at the present time. The incidence of diabetes in Baltimore is further indicated by the fact that in the thirty-six years since the opening of the Johns Hopkins Hospital, ending May 15, 1925, there were 1025 cases under treatment in the medical wards out of a total of 53,012 medical patients. Approximately 1 out of every 52 medical cases admitted to the hospital was a diabetic. The percentage of diabetic deaths of total deaths is lower in England and Wales than in the United States. It is much lower in Italy. The low mortality of Italy is exceeded only by that of Japan.

Etiology.—Race.—The disease appears to be about twice as common in the white as in the colored race. In the Johns Hopkins Hospital series of 1025 cases there were 132 in negroes, or 12.8 per cent., giving a ratio of 8 to 1. The ratio of white to colored admissions in the medical wards during this period has been about 4 to 1. It appears then that in Baltimore the white population is twice more liable to the disease than the colored. All authorities agree that the Hebrew race is particularly susceptible. Of Frerichs' 400 cases, 102 were Jews and Wallach demonstrated its greater frequency among the Hebrews of Frankfurt when from 1872 to 1890 the proportion of deaths from diabetes to the deaths from all causes was six times greater among the Jews than among the rest of the

inhabitants. Joslin believes that the increased susceptibility of Hebrews to the disease is due to their predisposition to obesity. It has been ascribed to greater instability of the nervous system, fondness for sweets, and overeating and sedentary habits, particularly among the better classes. Diabetes is very common among the educated and commercial classes in India, and Rose and Sen have shown that it is the Hindoos who chiefly suffer. The disease is comparatively uncommon in China and Japan. This is of great interest when we consider that carbohydrates constitute such a large part of the diet in these countries.

Heredity.—This is a factor in many cases. Richard Morton, who termed the disease *hydrops ad matulam*, or dropsy of the chamber-pot (Phthisiologia, 1689), records a family in which four children were affected, one of whom recovered on a milk diet and diascordium. Pleasants found only 6 cases, or 5.3 per cent., with a family history of diabetes, in the first 112 diabetics in Osler's Clinic at the Johns Hopkins Hospital. Statistics vary considerably. Grube found only 8 per cent. with a hereditary history; Bouchard's series showed 25 per cent., other statistics range between these. Joslin makes a distinction between "hereditary" and "familial" diabetics. The former include grandparent, parent, uncle, aunt and child. The latter embraces brothers, sisters and cousins and should not be considered hereditary cases. In his series of 2800 cases there were 417 hereditary cases or 15 per cent., and 189 familial cases or 7 per cent. Naunyn obtained a family history of diabetes in 15 per cent. of his cases. Obesity is often a feature in these hereditary cases. Heredity appears to be a favorable factor, as there is a concensus of opinion that the course is milder than when heredity does not play a part.

Infection and Conjugal Diabetes.—The possibility of one person contracting the disease from another by *infection* was first suggested by Schmidt in 1890. Among 2320 cases, he recorded 26 instances in which the disease appeared in apparently healthy persons, living in intimate association with diabetics. These were chiefly married females who had diabetes after nursing husbands suffering from the disease. These are cases of so-called "conjugal diabetes." Oppler and Kulz, in 1896, reported 47 married couples among 3489 diabetic patients or 1.08 per cent. Senator in the same year, stated that among 770 of his cases of diabetes, there were 9 instances in which a man and wife suffered from the disease. When one eliminates the influence of heredity, worry, obesity, and dietetic conditions in these cases, little evidence remains to support the hypothesis that diabetes can actually be contracted by one individual from another.

Age.—No *age* is exempt from the disease, but most authors agree that the largest number of cases occur between fifty and sixty years of age.

The incidence as to decades in the Johns Hopkins Hospital series of 1025 cases is shown in the following analysis:

1 to 10	11 to 20	21 to 30	31 to 40	41 to 50	51 to 60	61 to 70	71 to 80
8	68	110	177	240	254	148	20

The largest number of cases, 254 or 24.7 per cent., occurred in the sixth decade. These figures agree closely with those of Frerichs, Seegen, and Pavy, all of whom found the largest number of cases in the sixth decade,

their percentages being 26, 30, and 30.7 respectively. Wegeli, in an analysis of 102 cases in children under sixteen years, found the age distribution to be as follows: under one year, 3; one to five years, 26; five to ten years, 31; ten to sixteen years, 42. Stern mentions a case in which a child was apparently born with glycosuria, and in which recovery took place in eight months. Knox collected from the literature 16 cases in infants under one year of age.

Up to August 29, 1912, children under twelve years were admitted to the medical wards of the Johns Hopkins Hospital. The 8 cases in the first decade were admitted before that date. Since then all children up to that age have been admitted to the Harriet Lane Home. Through the courtesy of Dr. Howland I have been permitted to look up the number of cases of diabetes in his department. From August 29, 1912, to July 31, 1925, there have been 50 cases of diabetes under twelve years among 45,658 patients of the Harriet Lane Home. The youngest was fifteen months old. The oldest case in our series was seventy-five years of age. Four of the Harriet Lane Home patients were colored.

Diabetes is decidedly more common in the *male* sex. In our series of 1025 cases there were 626 males and 399 females. Of the 4672 deaths from the disease in the United States in 1900, 2650 were in males and 2022 in females. This disproportion is not so marked in childhood and extreme old age, when the figures are more nearly equal. Of Dr. Howland's 50 cases, 27 were males and 23 females. In the Johns Hopkins Hospital, series of the 132 cases in negroes, 81 were in females and 51 in males. This striking preponderance of diabetes in colored females is of interest, when in the total series of both races males markedly preponderated. Obesity, sedentary habits and employment as cooks no doubt play a part.

Social Status and Mental Strain.—In spite of the fact that the disease is often seen in its severest form among the poorer classes, it is undoubtedly more common in those of good *social position*. Not infrequently the onset of the disease is preceded by a history of fright, severe nervous strain, mental worry, and irritation. Mental strain undoubtedly is a potent factor. Those who have mental rather than physical work are more liable to the disease. Von Noorden states that 8 per cent. of his mild diabetics were in physicians. This frequency may be due to their facilities for recognizing the disease.

Obesity.—This plays a very important rôle. Diabetes occurs very frequently in persons who become stout during middle life. Joslin constantly emphasizes overweight as an important predisposing factor. In 1063 cases analyzed from this standpoint over 40 per cent. were obese. Frerichs had 59 cases of obesity among 400 diabetic patients, or 15 per cent. It occurred in 30 per cent. of Seegen's and in 45 per cent. of Bouchard's cases. Women are liable to become stout at the climacteric period, and are particularly prone to become diabetic at this time. Diabetes occurring in fat individuals is termed "lipogenous diabetes." When diabetes occurs in obese persons of middle age it is usually of a mild type, and the prognosis is more favorable, the glycosuria disappearing on a rigid diet. The obesity usually precedes the glycosuria by several years.

The fat diabetic is more common in private than in hospital practice. Occasionally obesity develops rapidly in young persons before the twentieth year. These subjects may also develop diabetes, which is always of a grave type.

Universally admitted as this connection between obesity and glycosuria is, the nature of the relationship between fat and carbohydrate exchange is not at all well understood. Von Noorden is of the opinion that the obesity is an early symptom of the diabetic condition, and that it develops long before glucose makes its appearance in the urine. Owing to the belief that the obesity is caused by the diabetic condition, he has given it the name "diabetogenous obesity." He believes that in every case of true diabetes not only the oxidation of carbohydrates, but also their conversion into fat is restricted. He says that it is conceivable that there are cases in which at first the power to burn up the sugar in the organism is alone interfered with, while the conversion of carbohydrates into fat still goes on. Under these circumstances the working or muscle cells of the body are richly bathed in a nutritive sugar solution; nevertheless they are starved because they cannot, or at least can only with difficulty, seize upon the sugar molecule, owing to deficient powers of oxidation. As a consequence there occurs a sort of tissue-hunger, which excites reflexly a sharper appetite and leads to the ingestion of a greater quantity of food. The latter results directly in an increased deposit of fat. According to von Noorden, such persons are diabetic, only they do not excrete sugar externally through the urine, but into the easily accessible layer of adipose tissue.

Obesity no doubt helps to explain conjugal diabetes, the prevalence of the disease in the Hebrew race, its frequency among the richer classes of society, and the greater susceptibility of colored females over colored males.

Dietary Excesses.—We might suppose that the prolonged excessive use of *carbohydrate food* would favor the development of diabetes but there seems no satisfactory evidence favoring this view. Cantani stated that the majority of his Italian patients subsisted largely on farinaceous food. He believed the diet was an important etiological factor. In Ceylon, where diabetes is common, large quantities of saccharine food are taken. The Chinese, on the other hand, rarely suffer from diabetes, although their diet consists chiefly of carbohydrates.

The statement is frequently made that the increased consumption of sugars since the passage of the Eighteenth Amendment in this country should increase the liability of the people to diabetes. At the present time there is no conclusive proof of this. A sufficient number of years has not yet elapsed to show whether this increased consumption has had any influence in fatiguing the islands of Langerhans.

Gout.—Some of the German clinicians have been inclined to the belief that the underlying metabolic disturbances causing gout may contribute to the development of diabetes. Grube, of Neuenahr, found that 16 out of 177 diabetic patients suffered from gout, and 23 had gouty parents (hereditary alternating gout). This proportion is probably unduly high owing to the fact that the waters at Neuenahr are especially recommended

for mild cases of diabetes in gouty patients. Von Noorden says that the connection between the two diseases may manifest itself in various ways. The patient may suffer from typical attacks of gout in middle life, and later the attacks cease and glycosuria appears. On the other hand, cases are observed in which attacks of gout alternate with glycosuria (diabetes alternans). In all these cases the diabetes is of a mild type and is compatible with a long life.

In this country, the association of the two diseases is uncommon. Gout existed in only one of our 1025 cases. Pratt found only one instance of glycosuria in his gout series.

Syphilis.—Most authorities are inclined to the view that syphilis rarely plays a part in producing diabetes. Joslin found a positive Wassermann reaction in only 1.6 per cent. of 1000 cases. Warthin and Wilson are strongly of the belief that syphilis is a potent factor. They find disease of the pancreas almost constantly in latent syphilis. They reported syphilitic lesions of the pancreas in 6 autopsies on diabetics. The question needs further elucidation.

Infectious Disease.—In certain cases the diabetic symptoms have begun shortly after one of the *infectious diseases*. Cases have followed typhoid fever, scarlet fever, cholera, diphtheria, and rheumatic fever. There seems no satisfactory evidence supporting the view that malaria is a contributory cause. Williamson thought influenza played a part in 6 out of 100 cases in which special inquiry was made into the previous history. Considering the prevalence of the acute infectious diseases there is no positive evidence at the present time that they play any great part in causing diabetes. The larger appetites and forced feeding during convalescence might be a factor.

Additional Factors.—In rare instances diabetes appears to be induced by *pregnancy*. The disease may manifest itself only during the pregnant period, being absent in the intervals. It is an occasional accompaniment of *Graves' disease* but more often a transitory glycosuria occurs. Lowered tolerance to carbohydrates in this disease has been demonstrated by numerous observers. Falkenberg reported cases in which glycosuria has followed extirpation of the thyroid. Marie, Strümpell and others observed it in *acromegaly*. Investigations of Cushing and others seem to indicate that a glycosuria probably occurs in all cases of this disease during the stage of hyperpituitarism. A transitory glycosuria occasionally supervenes after attacks of *gall-stone colic*. It may occur after the administration of a general anesthetic, and in other forms of narcosis. Asphyxia, by carbon monoxide or carbon dioxide, may cause a glycosuria, or even a true diabetes.

Glycosuria in Lesions of the Central Nervous System.—Although isolated observations had previously called attention to an association between certain lesions of the nervous system, and glycosuria or diabetes, it was Claude Bernard, who in 1849 first demonstrated this relation by his celebrated "piqûre" experiment. He showed that by puncturing a point in the floor of the fourth ventricle, situated between the centres for the pneumogastric and auditory nerves, a hyperglycemia, polyuria, and a transitory glycosuria occurred, lasting six hours in the rabbit,

and about forty-eight in the dog. Although this experiment has not been confirmed in man, it is not surprising that certain injuries to the central nervous system cause sugar to appear in the urine. Thus glycosuria or a true diabetes may follow severe *trauma*. Ebstein obtained a history of external injury in 6 out of 116, and Williamson in 6 out of 100 cases of diabetes. Ebstein collected 50 cases of traumatic diabetes from his own clinic and from the literature. In one-half of these, the head was the seat of the injury. Glycosuria is more liable to follow trauma in this situation. Injury to the pituitary or its stalk may account for the glycosuria. In other cases, injuries to the neck, liver, kidney region, and pubes have been followed by it. Ebstein thought that individual predisposition was a factor in determining the occurrence of diabetes in these cases. Glycosuria may also develop in the course of a traumatic neurosis. Before attributing glycosuria or diabetes to a traumatic neurosis it should be definitely demonstrated that glycosuria did not previously exist. In scarcely any of the reported cases has this been done. These cases occasionally are the subject of legal action.

Glycosuria or a true diabetes may occur in *organic lesions of the brain*, without Bernard's "diabetic centre" being necessarily involved. Glycosuria is not infrequent after *cerebral hemorrhage*. It rarely appears earlier than two hours after the apoplexy, and usually clears up within six days. Naunyn knew of only one instance in which the glycosuria passed over into a true diabetes—a case reported by Meyer. A true diabetes may be occasioned by a *tumor* of the pons, medulla, or cerebellum. Osler cited a case of a woman with anomalous cerebral symptoms and diabetes, in whom at postmortem a *cysticercus* in the fourth ventricle was found. Ebstein reported 4 cases in which there was a coincident occurrence of *epilepsy* and diabetes, but attributes the two diseases to the same cause. Similar observations have been made by Naunyn, Jacobi, and Lallier. Naunyn observed a case in chronic *encephalomalacia*. Observers agree in the comparative frequency of glycosuria, or a mild diabetes, in *general paresis*. Bond reports having found it in 10 per cent., and Strauss in 9 per cent. of their cases. Glycosuria is an occasional accompaniment of *tabes dorsalis* and *multiple sclerosis*. Tumors of the vagus and involvement of the nerve secondary to a caseated lymph gland have been associated with glycosuria. The latter is sometimes seen in severe cases of sciatica, but it must be remembered that neuralgias are not uncommon in diabetes. Isolated instances of disease of the abdominal *sympathetic ganglia* accompanied by glycosuria have been reported. Functional disturbances of the *autonomic nervous system* with its intimate relationship to the chromaffin system, including the adrenals, are now believed to be responsible for some cases of glycosuria.

Disturbances of the Endocrine Glands.—In the last three and a half decades extensive studies have been made by many investigators on the effect of the internal secretions of the various ductless glands on carbohydrate metabolism. These culminated in the brilliant work of F. G. Banting, of Toronto, and his associates, resulting in the discovery of insulin in 1922.

(*a*) *The Pancreas.*—Since Thomas Cawley, in 1788, recorded a case of diabetes in which the pancreas was atrophied and contained calculi, changes in the gland have been from time to time reported in this disease. In 1877, Lancereaux, on the strength of numerous clinical observations, described a special form of diabetes under the name of *diabète pancréatique ou diabète maigre*, in which emaciation was the striking feature, in contradistinction to *diabète gras*, in which the subject remains well nourished, and in which the pancreas was not thought to be involved. A great advance in our knowledge resulted from the publication by Minkowski and von Mering, in 1889, of the results obtained from the extirpation of the pancreas in animals. They demonstrated that complete extirpation of the pancreas in dogs and other animals was constantly followed by a fatal diabetes with all the classical symptoms including coma. It was found that when more than one-tenth of the gland was left intact diabetes did not occur. The ability of the liver and muscles to store glycogen was destroyed and only traces could be found in these organs after the administration of large quantities of carbohydrates. There is always a hyperglycemia, however, the amount of sugar in the circulating blood reaching as high as 0.5 per cent. within twenty-four hours. Minkowski and von Mering formulated the following hypotheses; either some substance which has an inhibitory action on sugar conversion collects in the blood after extirpation of the pancreas, or else, after this operation, some substance is wanting or function abolished which, under normal conditions serves to facilitate the conversion of carbohydrates.

Diabetes and Organic Diseases of the Pancreas.—Considering the part which we now know the islands of Langerhans play in the etiology of diabetes, it might at first appear surprising that the disease does not appear more frequently in serious destructive diseases of the pancreas. This failure of diabetes to develop in many of these cases, no doubt is due to the fact that the islands are more likely to be preserved wholly or partially intact than is the acinar portion of the glands. Before our knowledge of the part played by the islets, Naunyn was of the opinion that of all pancreatic lesions *pancreatic calculus* was the condition most likely to lead to diabetes. With this condition there is always an associated pancreatitis. Glycosuria or mild diabetes may develop in extensive *cancer* of the pancreas. The surprise is that it does not occur oftener. In an analysis of 31 cases in the medical wards of the Johns Hopkins Hospital, proved by operation or autopsy, mild, intermittent glycosuria occurred in only 3 instances. Others considered atrophy of the gland, *chronic interstitial pancreatitis*, the commonest pathological change. It is also surprising that glycosuria does not occur oftener in *acute hemorrhagic pancreatitis* with complete destruction of the gland. Seitz collected 100 such cases, in not a single one of which did glycosuria occur. This may be accounted for by the early death in most of these cases. Benda and Stadelmann reported a case with glycosuria. Sugar in the urine occasionally occurs in patients with *pancreatic cysts*.

The Association between Diabetes and Lesions of the Islands of Langerhans.—The year 1900 marked a new epoch in our knowledge of the etiology of diabetes when Opie published a pathological study on inter-

stitial pancreatitis in which he for the first time demonstrated a connection between disease of the islands of Langerhans and diabetes. His results were published more in detail in the following year. These groups of cells were first described by Langerhans in 1869. They are composed of columns of cells having no communication with the ducts of the gland, but being in intimate relation with a rich capillary net-work. They are about the size of a kidney glomerulus, measuring 0.2 mm. in diameter. The islands are situated for the most part in the centres of the ordinary gland acini, and are quite distinct, structurally and functionally, from them. They are distributed throughout the whole gland, but are more numerous in the tail than in the body or head. They are composed of small, irregular, polygonal cells having a round nucleus and homogeneous protoplasm.

Opie described two forms of chronic interstitial pancreatitis—an *interlobular* and an *interacinar* type. He found that certain of these cases, particularly of the interacinar type, suffered from diabetes. Histological examination of the pancreas in these cases showed extensive atrophy of the islands of Langerhans. These observations led him to make a systematic study of the pancreas in all cases of diabetes that came to autopsy. In a considerable percentage he found a hyaline degeneration of the island cells, those of the ordinary acini being uninvolved. Ssobolew, working independently, confirmed Opie's findings in 1901. W. G. MacCallum found that if a portion of the pancreas is separated from the rest of the gland and its duct tied it atrophies and leaves a tissue containing enlarged islands of Langerhans. If the remainder of the pancreas is removed this atrophied portion is able to ward off glycosuria, but if this is now removed glycosuria supervenes. Joslin and many other observers have confirmed Opie's work. All cases of glycosuria and diabetes do not show these changes in the islands, however. When a microscopic lesion is not demonstrable one must consider the possibility of a functional disturbance of these islands, just as we can have a functional disturbance of the acid-producing cells of the gastric mucosa.

At this point must be mentioned the group of cases of "bronze diabetes," occurring as a late manifestation of the affection known as *hemochromatosis*. This is characterized by a peculiar pigmentation of the skin and viscera, associated with a form of hypertrophic cirrhosis of the liver and extensive sclerotic changes in the pancreas, and accompanied in the late stages by a persistent glycosuria. Hanot and Chauffard first described these cases in 1882, and Hanot in 1886 suggested the name *diabète bronzé* and, as he considered the liver changes secondary to the diabetic condition, he gave the name *cirrhose pigmentaire diabétique* to this form of cirrhosis. The true nature of the affection was revealed in 1889 by von Recklinghausen, who described the disease under the name of hemochromatosis. He showed that the pigmentation of the skin and viscera is due to the deposition of an iron-containing pigment, hemosiderin, and a non-iron-containing pigment, hemofuscin.

Much investigation has been carried on with the view of determining the cause of this remarkable disease. The majority of opinion favors the view that it is dependent on some toxic agent leading to a breaking down of

the red blood cells with the deposition of the hemosiderin and hemofuscin in the various tissue cells. Mallory is of the opinion that it is due to the ingestion of copper and has produced the disease experimentally by feeding copper to animals.

The hemosiderin possesses a brown color and is deposited mainly in the cells of the liver, pancreas, lymphatic and sweat glands. The hemofuscin on the other hand, is finer, of an ochre-yellow color, and is found in the smooth muscle fibres of the stomach, intestines, blood and lymph vessels and occasionally in those of the urinary bladder and vas deferens. As a result of the deposition of the hemosiderin in the pancreas, this organ takes on a brownish, chocolate color, enlarges and become indurated and an extensive interstitial pancreatitis results. The disease may exist for years with diabetes as a terminal event, developing only when serious destruction of the islands of Langerhans occurs. Diabetes is the cause of death in the majority of these patients, the diabetic manifestations making their appearance one to two years before the fatal outcome.

Whenever hemochromatosis, either with or without diabetes, is suspected from the bronzed appearance and firm enlargement of the liver, the correctness of the diagnosis will be made much more probable by removal of a piece of skin and the demonstration of the iron-containing pigment in the sweat glands by the potassium ferrocyanide test, and of the ochre-yellow hemofuscin in the muscle fibres of any bloodvessels that may be present. A sugar tolerance test should always be made in these cases. A lower tolerance in the prediabetic stage is confirmatory evidence.

Reference has been made to the belief by Warthin and Wilson that *syphilitic* disease of the pancreas is an important causative factor in diabetes. This lacks confirmation in other quarters.

Naunyn, Grube, Laache, and Fleiner have drawn attention to the frequency in the association between *arteriosclerosis* and diabetes. Nutritional changes in the pancreas, due to sclerosis of the pancreatic arteries, has been suggested as the assignable cause. Fleiner reported a case of diabetes in a patient with general arteriosclerosis in which there was a diffuse interstitial pancreatitis with marked thickening and obliteration of the branches of the pancreatic artery.

Changes in the Islands of Langerhans in Diabetes.—Two totally distinct processes take place in the pancreas in diabetes and can be demonstrated at autopsy. The first of these constitutes the lesions causing the diabetes and is manifested by changes resulting from an acute, subacute, or chronic pancreatitis. It presents itself in the formation of fibrous tissue throughout the pancreas, but particularly in the islands, where it manifests itself as a hyaline degeneration. Many severe cases show almost complete destruction of the islands. In some instances this striking destruction is absent and the islands may appear almost normal. In these cases we must consider the possibility of a functional disturbance of the islands.

The second change is what Allen has termed a hydropic degeneration. These changes are found in partially depancreatized animals as well as in the human diabetic. They are the consequence of, and not the cause of the disease. The changes are characterized first by a disappearance of the

granules in the cells of the islands, then a swelling of the cells with fluid, and finally a disappearance of the islands. Allen is of the opinion that this hydropic degeneration in partially depancreatized dogs is a specific diabetic phenomenon produced solely by overstrain of the function of the cells by diets in excess of the weakened assimilative power. It is believed that considerable regeneration of the destroyed islands may occur under certain circumstances.

History of the Discovery of Insulin.[1]—As far back as 1892 Lepine, of Lyon, advanced the view that diabetes in man, and in animals after extirpation of the pancreas, is due to the failure of the pancreas to produce a "glycolytic ferment," which occurs as an internal secretion. After the discovery by Opie and Ssobolew of the intimate relation between lesions of the islands of Langerhans and diabetes, various attempts were made to isolate from these islands their internal secretion. In 1908 Zuelzer almost succeeded. He obtained an alcoholic extract from the pancreas of recently fed animals and found that when injected intravenously it reduced the hyperglycemia of epinephrinized animals and also in one depancreatized animal. Owing to the severe reactions following the injections it could not be used in human diabetics. Similar attempts were made by many others but none succeeded in securing a sufficiently potent, non-toxic extract that could be used in human individuals. It is of historical interest that the name *insulin* was first suggested for the anti-diabetic hormone of the islands by Sir E. Sharpey Schäfer in 1916.

When others failed, it remained for F. G. Banting, of Toronto, and his group of co-workers Best, Collip, Macleod, Fletcher, Campbell and Noble to succeed in 1922. Their work stands forth as one of the most brilliant successes in the realm of therapeutics. Banting's results were not obtained in a haphazard way but by utilizing an important observation previously made. Banting and Best say: "The hypothesis underlying this series of experiments was formulated by one of us in November, 1920, while reading an article dealing with the relation of the isles of Langerhans to diabetes. From the passage in this article, which gives a résumé of degenerative changes in the acini of the pancreas, following ligation of the ducts, the idea presented itself that since the acinous, but not the islet tissue, degenerates after this operation, advantage might be taken of this fact to prepare an active extract of islet tissue. The subsidiary hypothesis was that trypsinogen, or its derivatives, was antagonistic to the internal secretion of the gland. The failures of other investigations in this much-worked field were then accounted for."

Standardization of Insulin.—The amount of insulin necessary to reduce the blood sugar of a 1 kilogram rabbit, starved about twenty hours, to 0.045 per cent. or to produce convulsions in three hours was agreed upon by the workers to represent 1 unit of insulin. Since November, 1923, the new international unit established by the Health Section of the League of Nations has become generally adopted. It represents one-third the

[1] For a comprehensive discussion of the insulin question the reader is recommended to consider the following references. Both contain an extensive bibliography to date.

Insulin.—W. R. Campbell and J. J. R. Macleod: *Medicine*, 1924, 3, 195–308.

Insulin and its Use in Diabetes. W. R. Campbell and J. J. R. Macleod. The Waverly Press, Williams & Wilkins Company, Baltimore, 1925.

quantity of insulin required to lower the blood-sugar of a 2 kilogram rabbit to the convulsive limit, 0.045 per cent.

Practical experience of three and a half years by many clinicians has proved the inestimable value of this remedy. Many lives have been saved and the outlook of the diabetic is now a much happier one than in the pre-insulin days. Its use results in the ability of the system to burn sugar, causes the disappearance of hyperglycemia and glycosuria, raises the respiratory quotient of the diabetic, and enables him to burn his ketone bodies by increasing the ability to burn sugar (as fatty acids are only burnt in the sugar furnace) and thus infinitely lessens the danger of death from coma. The liver and muscles regain their power to store glycogen.

An important fact has been established by the combined work of numerous observers. It has been found that 1 unit of insulin is capable of burning 1.5 gm. of glucose. This is important in determining the required dosage in any individual diabetic. after the total daily excretion of sugar is determined on a maintenance diet.

Other Sources of Insulin.—Besides the mammalian pancreas the principal islets of bony fishes may be utilized to obtain insulin. It has been recovered from the angle or devil fish, sculpin, cod, pollock and halibut. It has also been obtained from clams, yeast, onion tops, and even from grass and potatoes. Collip believes that these extracts differ somewhat from insulin and to them has applied the name *glukokinin.*

The Chemistry of Insulin.—In 1925, Abel and Geiling[1] published a very important preliminary report of their work on the chemistry, purification and standardization of insulin. They worked with the Lilly product. They have demonstrated conclusively that one of the important ingredients is sulphur in an unstable form, and believe that insulin is an unstable sulphur compound. They believe that the potency is dependent on the amount of "sodium carbonate sulphur" it contains. They say "We wish to point out that if the labile sulphur is a pivotal element of insulin, then we possess in it a sulphur compound of high specificity, and one that plays a paramount rôle in the normal metabolic changes which the carbohydrates undergo during their utilization in the animal economy. In this connection too, the question suggests itself as to what extent, if any, the islets of Langerhans are dependent upon the presence in our food of a special labile sulphur compound, a precursor for the elaboration of the hormone, in the absence of an adequate supply of which, pathological alterations in the cells of the islets of Langerhans would take place. Should a connection of this nature be ultimately established, there would come to light an important and hitherto unrecognized etiological factor in the causation of diabetes mellitus."

In a verbal communication Dr. Abel told the writer that deficiency of this labile sulphur may mean for the islets what utilizable iodine means to the thyroid for its proper function. This suggestion seems to be of the utmost significance. Abel and Geiling have also so purified the commercial insulin that 1 mg. represents 80 units, a most important contribution from a therapeutic standpoint.

[1] *Jour. of Phar. and Exp. Ther.*, 1925, **25**, 423.

(*b*) *The Adrenals and Chromaffin System.*—The chromaffin system is composed of those cells in the body which have an affinity for chromic acid stains. These cells are contained, for the most part, in the adrenals. They are found accompanying the sympathetic nerves; they occur also in the retroperitoneum, and they are grouped together in the pelvis to form the so-called Zuckerkandl organ. All these cells apparently possess the same functions.

Clinically, we know of no organic disease of the adrenals that produces glycosuria or a true diabetes. Yet the adrenal hormone powerfully influences carbohydrate metabolism. F. Blum, in 1901, was the first to produce glycosuria in dogs by the intravenous injection of epinephrine. These results have been amply confirmed by Herter and many others. For a long time it was not known how this glycosuria was brought about. Through the work of Zuelzer, von Noorden and his fellow investigators, it has been demonstrated that the glycosuria following epinephrine administration is probably due to an increased mobilization of the glycogen in the liver, or in other words to an increased glycogenolysis, causing a temporary increased production of glucose and consequent hyperglycemia. Falta, Eppinger and Rudinger have shown that the adrenals and chromaffin system produce a hormone that acts as an "accelerator" so far as carbohydrate metabolism is concerned. It is directly antagonistic in its action to the hormone of the pancreas, which inhibits glycogenolysis. In health we are supposed to have an even balance in the action of these two hormones and consequently the sugar in the circulating blood remains within normal limits. This balance may be disturbed in many ways producing hyperglycemia and glycosuria. There is an intimate relationship between the sympathetic nerves and the chromaffin system. In functional neuroses the latter system is stimulated through the autonomic nervous system and we have an overproduction of the accelerator hormone and consequent hyperglycogenolysis with resultant glycosuria. It seems probable that the glycosuria following certain of the lesions of the central nervous system is produced as a result of overstimulation of the adrenals through the sympathetic nerves. The nervous impulses pass down by way of the left splanchnic to the left adrenal and thence to the right. The glycosuria following Claude Bernard's "piqûre" experiment has been shown to be really of adrenal origin. The stimulation of the medulla is passed on to the adrenal by the sympathetic. If the left splanchnic is previously cut, glycosuria does not follow the piqûre experiment. The fact that there is hypoglycemia after extirpation of the adrenals as well as in severe cases of Addison's disease shows the influence of these glands on carbohydrate metabolism.

Patients with vagotonia are very sensitive to epinephrine and develop a considerable glycosuria with the injection of even 1 mg. In those with sympathicotonia it takes a much larger dose to produce glycosuria. Von Noorden believes that the vagus and sympathetic types are also present among diabetics. In one group the glycosuria is markedly increased by psychic or nervous influences, while in the other, these influences do not affect it. The increased glycosuria in the former is supposed to be due to

the mobilizing action of the increased epinephrine secretion on the glycogen of the liver.

(*c*) *Hypophysis.*—Clinical experience for a long time pointed to a relationship between the pituitary gland and carbohydrate metabolism. It was long known that tumors in the region of the hypophysis, particularly in acromegaly, produced glycosuria. Out of 176 cases of acromegaly reported up to 1908, Borchardt found that glycosuria occurred in 35.5 per cent. We owe to Cushing and his co-workers the demonstration of the fact that it is the secretion of the posterior lobe of the pituitary that affects carbohydrate metabolism. By removing the posterior lobe and a part of the anterior lobe in puppies the animals fail to grow properly; the sexual apparatus remains undeveloped; they become obese and their tolerance for saccharose becomes enormously increased. This hypopituitarism is an experimental counterpart of a type of infantilism in the human individual described by Fröhlich as "dystrophia adiposogenitalis." Cushing showed further that the subjects of "Fröhlich's syndrome" have an enormously increased tolerance for carbohydrates. The latter, instead of being completely metabolized, become converted into fat. The patients with this type of infantilism have hypoplasia of the entire hypophysis, including the posterior lobe. Their tolerance for carbohydrates can be lowered and their adiposity diminished by administering extract of the posterior lobe.

The secretion of the posterior lobe of the hypophysis reaches the third ventricle by the infundibulum. It becomes mixed with the cerebrospinal fluid, and is probably absorbed into the circulation by way of the subdural spaces. It probably exerts its influence on carbohydrate metabolism by producing hyperglycogenolysis. It may do this directly. On the other hand, it may produce its effect by stimulating the hormone of the adrenals or by inhibiting the hormone of the pancreas. The fact remains that a hyperglycemia and glycosuria can be produced by the injection of posterior lobe extract into dogs. Simple manipulation of the stalk at operation frequently produces a glycosuria. This is no doubt due to increased absorption of posterior-lobe secretion.

The glycosuria following fractures of the base of the skull may be in some cases due to disturbance of the posterior lobe secretion. In pregnancy there are certain signs of hyperpituitarism and some of the glycosurias of pregnancy may be due to hypersecretion of the posterior lobe during temporary hyperplasia of the whole gland.

In the late stages of acromegaly (hypopituitarism) the subjects become obese, and in this stage of the disease there is an increased tolerance for carbohydrates. The adenomas of the anterior lobe, causing the acromegaly, produce a hypoplasia of the posterior lobe, thus explaining this increased tolerance to starches and sugars and the consequent tendency to adiposity. The discrepancies in the results reported concerning the presence or absence of glycosuria in acromegaly probably depend entirely upon the stage of the disease at which the investigation was made. The probability is that all acromegalics in the early stages have either a glycosuria or a diminished tolerance for carbohydrates.

(*d*) *Thyroids and Parathyroids.*—Those who have had a wide experience with diseases of the thyroid gland have been impressed with the fact that in hyperthyroidism and hypothyroidism there is a marked disturbance of carbohydrate metabolism. Many have observed that spontaneous glycosuria is not uncommon in exophthalmic goitre. Further, it has been shown that the administration of small amounts of carbohydrate in this condition often causes a temporary glycosuria. In other words, in overactivity of the gland the tolerance for carbohydrates is reduced.

On the other hand, in hypothyroidism, cretinism and myxœdema, the occurrence of spontaneous glycosuria is extremely uncommon. Hirschl found in an outspoken case of myxœdema that the administration of 200 to 500 gm. of grape-sugar did not produce alimentary glycosuria. Thus carbohydrate tolerance was increased two to five times. The administration of epinephrine is said by Falta not to produce glycosuria in thyroidectomized dogs. MacCallum demonstrated that the glycosuria following pancreatectomy is diminished by extirpation of the thyroid. Extirpation of the thyroid raises the tolerance of animals for sugar, so that alimentary glycosuria is produced with difficulty, provided that the parathyroids are not disturbed. John H. King has produced experimental evidence tending to show that the expressed juices from the thyroid and pancreas break up glucose in much the same way as Cohnheim demonstrated for the juices expressed from the muscles and pancreas. Grey and De Sautelle have shown that the glycosuria in animals following administration of ether or chloroform is markedly diminished if the thyroid has been previously removed, demonstrating, as they believe, that when the restraining influence of the thyroid is removed the pancreas is more efficient for carbohydrate metabolism.

Eppinger, Falta, and Rudinger have shown that the parathyroids possess an opposite effect to that of the thyroids on carbohydrate metabolism. Underhill and Hilditch demonstrated that after excision of three of the four parathyroids in the dog the tolerance of the animal for sugar was greatly lowered, and that complete thyroparathyroidectomy, besides causing tetany, gave rise to glycosuria.

Diabetes and Organic Diseases of the Liver.—When one considers what an important part the liver plays in carbohydrate metabolism—being the great glycogen reservoir—it would be natural to expect that organic lesions of the liver would frequently be the cause of diabetes. Clinical experience, however, teaches us that the most extensive disease of the liver, such as carcinoma and cirrhosis, may occur without any glycosuria. Naunyn was the strongest advocate of a "liver diabetes," in which the diabetes is due to the organic change in this gland. He described cases of diabetes attributed to *cirrhosis* of the liver and to the liver disturbances accompanying *gall-stones*. He also drew attention to the frequency with which he found glycosuria in individuals with enlarged livers, caused by *passive engorgement* secondary to cardiac disease. There does not seem to be sufficient evidence to justify the opinion that a true "liver diabetes" exists. Until a large number of cases of diabetes with organic disease of the liver and without microscopic evidence of disease of the islands of Langerhans are reported, we must support this contention.

Renal Diabetes.—The most characteristic type of renal diabetes is that known as "phloridzin diabetes," experimentally produced by the administration of phloridzin to man or animals. In 1886 von Mering discovered that when phloridzin is administered by mouth or subcutaneously in man or animals a temporary glycosuria results. The amount of sugar in dogs may reach 18 per cent. The glycosuria continues in animals fed on nitrogenous diet, or in men when fasting, indicating that the sugar is in part manufactured from proteins. An important fact is that no hyperglycemia exists. That the glycosuria results from the phloridzin causing certain changes in the renal cells rendering them more permeable to glucose, is indicated by the fact that there is no increase of glucose in the blood; by failure of a hyperglycemia to occur after ligaturing the ureters or excising the kidneys; and by the observation of Zuntz, who found that when phloridzin is injected into one renal artery, glucose is excreted by the corresponding kidney immediately, while it does not appear in the urine of the opposite kidney until half an hour later, that is, until after it reaches that kidney through the general circulation.

For some time doubts were expressed whether, clinically, the "renal diabetes" of Jacobi actually occurs. While the cases are undoubtedly rare, there has been a sufficient number reported by competent observers that there can be no doubt that such cases do occur. The persistent excretion of considerable amounts of sugar in an otherwise apparently healthy person should rouse suspicion, if repeated analyses of the blood-sugar fail to show a hyperglycemia. Renal diabetes, like diabetes mellitus, is both hereditary and familial. The disease may exist for a great many years without any evidence of kidney damage from the excretion of sugar. One of Billing's cases was observed by Joslin twenty-seven years after the first observation.

Miscellaneous Factors.—Transitory glycosuria occasionally occurs in the course of acute fevers. It is not uncommon after the administration of ether, less so after chloroform. Hofmeister has produced a "hunger-diabetes" in dogs by cutting off all food for a few days. A clinical analogy to this is the glycosuria which occasionally occurs in severe cachexias and anemias. Patients suffocated by smoke or poisoned by carbon monoxide may have a temporary glycosuria.

Disturbances of Metabolism in Diabetes. The discovery of insulin has solved most of the mysteries connected with the physiology of the carbohydrates in health and in diabetes. For a better understanding of the diabetic problem it may be well to review briefly the sources from which glucose is derived in the food and the fate of the carbohydrates in normal metabolism.

The *hexoses* mainly concern us in a discussion of both normal and pathological carbohydrate metabolism. The hexoses, in general terms, may be described as carbohydrates, the molecules of which contain the carbon atoms to the number of six or multiples thereof, and the hydrogen and oxygen atoms in the proportion in which they form water. They are classified according to the number of carbon atoms they contain:

1. The *monosaccharides*, or *glycoses*, having the general formula $C_6H_{12}O_6$. These include grape-sugar, also called dextrose or glucose

(dextrorotatory); fruit-sugar or levulose (levorotatory); galactose and mannose (both dextrorotatory). All these ferment and reduce alkaline copper-sulphate solutions.

2. The *disaccharides*, or *saccharoses*, possessing twelve atoms of carbon in the molecule, and having the formula $C_{12}H_{22}O_{11}$. These are formed by the combination of two molecules of a monosaccharide with the loss of a molecule of water. They include cane-sugar or saccharose; milk-sugar or lactose; and maltose. With the exception of cane-sugar, all reduce alkaline copper-sulphate solutions. All are dextrorotatory, but do not ferment without being split up by dilute mineral acids, etc.

3. The *polysaccharides*, or *amyloses;* these are the anhydrides of a combination of many molecules of monosaccharides, and possess the general formula, $(C_6H_{10}O_5)n$. They include starch, glycogen, and dextrin (all dextrorotatory); inulin (levorotatory); cellulose, and animal gum (inactive). They do not reduce alkaline copper-sulphate solutions and do not ferment without being previously split up.

Normal Carbohydrate Metabolism.—(*a*) *Formation of Glucose from Carbohydrates.*—The carbohydrates in the food undergo a series of changes during digestion, as a result of the action of the diastatic ferments in the saliva, pancreatic juice, and succus entericus. Possibly some changes also occur in the process of absorption. Starch, the most abundant article in our dietary, is eventually converted into maltose, or maltose and dextrin, after passing through a series of intermediate stages. The maltose and dextrin are further converted into dextrose by the sugar-splitting enzymes of the intestinal mucous membrane. Cane-sugar is hydrolyzed into dextrose and levulose, and milk-sugar probably undergoes a similar change to dextrose and galactose, although of this we are not so certain. The carbohydrates of our food are eventually absorbed in the form mainly of dextrose (glucose) or dextrose and levulose. These sugars are absorbed directly into the portal capillaries and not into the lymphatics. As a result of carbohydrate digestion the portal vein conveys to the liver a stream of sugars consisting mainly of dextrose, but also of smaller quantities of levulose and galactose, and there, by a process of dehydration, the liver-cells convert them into glycogen as follows: $C_6H_{12}O_6 - H_2O = C_6H_{10}O_5$. The surplus that is not required for the immediate use of the economy is stored up in the liver as glycogen. According to the generally accepted view of physiologists, this glycogen is reconverted into glucose by a special enzyme called *glycogenase* which is found not only in the liver cells but also in the blood and lymph. This glucose reaches the general circulation by the hepatic veins, and is conveyed to the muscles and other tissues, where it is oxidized, producing heat and energy. It must be remembered that the muscles also constitute a store-house for glycogen.

(*b*) *Formation of Glucose from Ingested and Body Proteins.*—A great deal of information has been acquired concerning the relation between the urinary nitrogen and sugar elimination in the fasting and meat-fed diabetic organism. The dextrose to nitrogen ratio (D : N) is a key to the problem of the quantity of sugar which can be derived from protein metabolism. Minkowski discovered that depancreatized dogs, whether

fasting or fed on meat, showed a constant elimination of 2.8 gm. of dextrose for each gram of nitrogen in the urine. This ratio (D:N::2.8:1) was the average obtained from several dogs on twenty-two different days. He showed that 45 gm. of glucose is formed from every 100 gm. of protein metabolized in the body. Nolan and Lusk have demonstrated that in phloridzin diabetes the D:N ratio is 3.56:1. Falta has shown that this same ratio may exist in dogs after the removal of three of the parathyroids and the pancreas. It is now generally conceded that the D:N ration in most diabetics who have no tolerance for carbohydrates is 2.8:1, while in a few cases it has been found to be 3.65:1. The former represents a formation of 45 gm. of dextrose from 100 gm. of meat protein, the latter one of 58 gm. of sugar from meat protein. The dextrose in the 2.8:1 ratio is spoken of as α-dextrose, whereas that in the 3.65:1 ratio is called β-dextrose. The β-dextrose represents the additional 13.6 per cent. of protein, when the ratio 3.65:1 exists. The ratio depends upon the combustion or non-combustion of the β-dextrose. If the latter burns, it must do so as a complex, for as free dextrose it would be eliminated in the urine (Lusk). The formation of dextrose from protein is now a well-established fact. Further evidence is afforded by the fact that severe diabetics often excrete sugar when on a starvation diet. In calculating the diet of a diabetic it is most important to remember that in the metabolism of the protein molecule 58 per cent. of it yields carbohydrate.

(*c*) *Formation of Dextrose from Fat.*—The fat of the food and tissues is also a potential source of carbohydrate. The fat molecule yields 10 per cent. of glycerol which the economy converts into sugar. This must also be taken into account in the adjustment of a diabetic diet.

The liver is capable of storing up glycogen to the extent of 14 per cent. of its own weight. The amount it contains depends on several factors. Prolonged fasting, continuous physical exertion, and high temperature rapidly deplete its supply of glycogen. The latter is greatest in amount on a diet rich in carbohydrates. The liver is not the only seat for the storage of glycogen, however. The other great reservoir is the muscular system; and it is estimated that the quantity in the muscles practically equals that stored in the liver. When conditions favor the depletion of the supply of glycogen it is found that the muscles give up their supply much less readily than does the liver. The source of the muscle glycogen is not definitely known, but presumably it is formed from the glucose brought to the muscles by the blood.

Form in Which Sugar Circulates in the Blood.—It is not definitely known whether dextrose normally circulates in the blood as such or in combination. Loewi believes it is in loose combination with a colloid substance. He holds that the colloid sugar cannot pass through the glomerulus. If for any reason, sugar accumulates in the blood above the combining power of the colloid, then the crystalloid dextrose readily passes through the kidney. Lusk supports Loewi's view.

Considerable work has been done on the constitution of the glucose molecule in the blood of normal and diabetic patients. Ordinary chemically produced glucose exists in two forms, as α-, and β-glucose. The English observers, Hewitt and Pryde, first suggested that the glucose of

the blood of normal animals and man possessed a different constitution, and discussed a hypothetical form to which they gave the name γ-glucose in 1920. In 1923, Winter and Smith, of Cambridge University, found that the blood of normal individuals possessed a lower value for rotatory power than for reduction power and believed that it corresponded with Hewitt and Pryde's γ-glucose. They believed that the glucose in the blood of individuals with severe diabetes was in the form of α- and β-glucose, and advanced the view that the failure to find γ-glucose was due to the absence of a specific enzyme. Winter and Smith's results have been confirmed by Eadie in Macleod's laboratory.

In 1924 and 1925, Lundsgaard and Holbøll, of Copenhagen, showed that by adding insulin and fresh muscle tissue *in vitro* to a solution of α, β-glucose a transformation of part of the glucose into a new, hitherto unknown, form of glucose takes place. It possesses a lower specific rotatory power than that of α, β-glucose. They found this sugar in the blood of 11 normal individuals, thus confirming Winter and Smith's work. They believe it is the first link in the chain of the transformation of glucose in normal carbohydrate metabolism. They discuss the question of the identity of this glucose with γ-glucose, but prefer, for the time being, to call it *new-glucose*.

Blood Sugar and the Renal Threshold.—In the normal individual, through the mechanism of the glycogenic function of the liver, the determination of the blood-sugar at all hours of the day reveals the fact that the percentage remains within a very narrow range. Normally, after a meal rich in carbohydrates the excess of sugar is stored in the liver as glycogen and remains there to be called on by the muscles and other tissues to produce heat and energy by oxidation. The normal amount of blood-sugar on a fasting stomach, that is, before breakfast, is on an average 0.1 per cent. Gray compiled the average of 431 observations from many sources and found it to be 0.09 per cent., the minimum being 0.04 per cent. and the maximum 0.16 per cent.

The *renal threshold*, that is the degree of concentration of sugar in the circulating blood before the sugar "leaks over" into the urine is generally agreed to be about 0.16 to 0.18 per cent.

(*d*) *Blood-sugar in Diabetes.*—The characteristic feature of the metabolic disturbance of diabetes is the development of a hyperglycemia. When the glucose concentration of the blood reaches above 0.16 to 0.18 per cent., certainly 0.2 per cent., glycosuria is most likely to occur. It is an interesting observation, however, that occasionally in known diabetics the renal threshold is found to be much higher. It is not rare to find aglycosuria in diabetics with a blood-sugar near 0.2 per cent. or higher. In severe diabetics the percentage of sugar may reach very high levels. The highest in our Johns Hopkins Hospital series was 0.9 per cent. in a severe coma case. The highest value reported in the literature was 1.40 per cent. by Olmsted, also in a patient in coma.

(*e*) *Alimentary Glycosuria.*—Although Folin and Berglund do not approve of this term, it is generally applied to those instances in normal individuals in which a glycosuria occurs following a meal very rich in some form of sugar. The liver is supposed to be capable of storing about

300 gm. of glycogen. When this storage capacity is reached after a meal rich in sugar of some form or other, the glucose accumulates in the circulating blood and when it reaches above 0.16 to 0.18 per cent. a transitory glycosuria results. In the normal individual starches may be taken in unlimited amounts without sugar appearing. The conversion and absorption of the starches takes so much time, that a sudden hyperglycemia and glycosuria are impossible. The quantity of any form of sugar that can be ingested without its appearing in the urine is designated by Hofmeister as the *assimilation limit*. This varies in normal persons according to the form of sugar ingested.

Glucose Tolerance Tests and Blood-sugar Curves in Normal and Diabetic Individuals.—Various methods have been advised for determining the glucose tolerance in any individual case in which a lowering may be suspected. The customary procedure in the past has been to give 100 gm. of glucose on a fasting stomach before breakfast, without any very specific directions as to the amount of water in which it is dissolved. It would seem better that the weight of the individual should be taken into consideration in determining the amount of glucose that is given. It would also appear to be important that the amount of water in which the glucose is dissolved should be determined on a definite basis. If large quantities of water are given the absorbed water could easily increase the bulk of the blood and consequently lower its percentage of sugar.

The following is the procedure carried out in the wards of the Johns Hopkins Hospital. The patient is weighed and 1.75 gm. of glucose given per kilo ($2\frac{1}{5}$ pounds) body weight. The amount of water is 2.5 cc. for each 1.75 gm. of glucose required. With the stomach empty, before breakfast a specimen of blood from an arm vein is taken for sugar determination. The glucose solution is then given by mouth. Specimens of blood are taken at half hour, one hour, two and three-hour intervals and samples of urine every hour for three hours. The blood-sugar determinations are then made and the urine examined qualitatively and quantitatively for sugar. If a glycosuria occurs with this procedure a lowered tolerance may be considered to exist.

In normal individuals Jacobson in giving 100 gm. of glucose found that the blood-sugar curve begins to rise in five minutes. The increase reaches on an average 0.14 per cent. in half an hour, 0.12 per cent. in one hour, 0.11 per cent. in two hours, but in three hours the percentage drops to slightly below normal or 0.09 per cent.

The tolerance test administered in diabetic patients raises the blood-sugar curve higher and for a longer period than in normals. Following 100 gm. of glucose, Joslin found the blood-sugar of 40 diabetic patients with a normal, fasting blood-sugar rose to 0.18 per cent. in half an hour, 0.20 per cent. in one hour, 0.15 per cent. in two hours, and 0.10 per cent. in three hours.

Metabolic Changes in Diabetes.—The striking disturbances of metabolism in diabetes are universally recognized now to be due to the failure of the islands of Langerhans to produce insulin. The severity of the metabolic disturbances are directly dependent upon the degree of this disturbed

function, whether it be due to functional or organic disease of the islands. These metabolic disturbances may be briefly stated to be as follows.

(*a*) *Hyperglycemia.*—The metabolism of the carbohydrates, which are the most readily warehoused of all foodstuffs, is the first to become affected. As the amount of insulin produced lessens, the inability of the tissues to burn sugar advances *pari passu.* This leads to a hyperglycemia and resultant glycosuria. As the diabetic disturbance increases, the ability of the liver to store glycogen progressively decreases also, so that in the severest cases there may be no glycogen found in the liver whatever, similar to the condition found in the completely depancreatized dog.

This inability of the tissues to burn sugar is well manifested by the determination of the *respiratory coefficient.* This is obtained by dividing the amount of carbon dioxide produced by the amount of oxygen required by a patient on a given diet for a given period of time. In the normal individual, the respiratory quotient for an exclusive carbohydrate diet is unity or 1; for protein 0.81; and for fat 0.71. In other words it requires much more oxygen to burn fat and protein than it does carbohydrate. In the severe diabetic, owing to the inability to burn carbohydrate, the greater difficulty to burn protein, and owing to the heavy production of the fatty acids, the respiratory quotient may fall to 0.73 or even to 0.69, which are dangerous levels.

(*b*) *Disturbance of Protein Metabolism.*—It must be remembered that in the normal metabolism of the protein molecule 58 per cent. is yielded as available carbohydrate.

So long as a diabetic is still capable of warehousing moderate amounts of carbohydrates there is no special disturbance of *protein metabolism.* While in the healthy individual, and in mild diabetics, the supply of carbohydrates derived from protein metabolism can be made use of to protect the tissues from further destruction, in the severe type this is not the case, for when the protein sugar is withdrawn from the tissue cells there is a large increase in protein metabolism, and consequently in the nitrogen output in the urine. Mendel and Lusk found in a severe diabetic that the ingestion of broths containing 7.7 gm. of nitrogen was followed by an elimination of 21.7 gm. of nitrogen in the urine, or a loss of body nitrogen of 14 gm., and that nitrogen equilibrium could only be maintained by giving 27 gm. of protein nitrogen in the food. Minkowski, Falta, and Lusk have shown that the D:N ratio in diabetics who have completely lost their power to warehouse carbohydrates is constant, either 2.8:1 or 3.65:1, no matter how much protein is given, and is in no way dependent upon variations in the amount of fat in the diet. Further evidence of the disordered protein metabolism is found in the great increase in the quantity of the total urinary nitrogen and especially of the high relative increase in the ammonia nitrogen in severe diabetics. In severe cases the urinary nitrogen may reach 25 to 30 gm. daily in contrast to about half this amount for the normal individual.

(*c*) *Disturbances of Fat Metabolism.*—In health the lipoids (fat) are normally present in the blood in four forms, (1) as *glycerides of the fatty acids,* usually oleic, palmitic and stearic; (2) lecithin, a compound of

glycerine with 2 molecules of fatty acids and 1 molecule of phosphoric acid, which is in turn combined with 1 molecule of cholin; (3) *cholesterol*, a secondary alcohol belonging to the terpene series; and (4) *cholesterol esters*, combinations of cholesterol with a fatty acid, usually oleic or palmitic acid. In a consideration of the lipoids of the blood one usually refers to (1) the total fatty acids, including under this term the fatty acids of the glycerides, the fatty acids in lecithin, the fatty acids in the cholesterol esters; (2) lecithin; and (3) the cholesterol existing free or combined with fatty acid as a cholesterol ester. The total fatty acids normally represent the predominant form, about 50 per cent., in which fat appears in the blood. According to Joslin the normal percentage of fatty acids in the blood is 0.3 per cent.

In the normal individual for the complete combustion of fat it is necessary that a certain amount of carbohydrate must be burned simultaneously. With increasing impairment of the function of the islands of Langerhans in diabetes a point may be reached where there is complete inability of the tissues to burn sugar, with a consequent corresponding inability to burn fat, leading to a great increase in certain of the fatty acids in the blood, with the attendant risk of the development of coma. What happens may be best expressed in the words of Macleod. "For the thorough combustion of fat in the animal body a certain amount of carbohydrate must be simultaneously burned. Fat evidently is a less readily oxidized foodstuff than sugar; it needs the fire of the burning sugar to consume it. If the carbohydrate fires do not burn briskly enough, the fat is incompletely consumed; it smokes, as it were, and the smoke is represented in metabolism by the ketones and derived acids."

The fatty acids which accumulate in the blood and tissues in diabetes are acetoacetic (diacetic) and β-oxybutyric acid, which are related to acetone, and which are derived from fatty acids by a faulty metabolism. When these accumulate in the blood a condition first called "acidosis" by Naunyn occurs. This toxic state is now often referred to as"ketosis," owing to the fact that acetone, diacetic acid and β-oxybutyric acid are known collectively as the "ketone" bodies. Although the bulk of the ketone bodies are derived from fat a small amount originates also in the amino-acids of the protein molecule.

Total Metabolism in Diabetes.—A great deal of work on the total metabolism of diabetics was been done by Wilder, Boothby and Beeler at the Mayo Clinic and by Benedict and Joslin at the Carnegie Nutrition Laboratory at Boston. According to Joslin, it varies greatly, and in his belief is dependent in a considerable measure on the form of dietetic treatment used. In the cases studied between 1908 and 1914 the metabolism was found to be on an average 12 per cent. *above* normal. This was the period when patients were placed on a low carbohydrate and relatively high fat-protein diet. Similar patients since 1914 show a metabolic rate of 11 below normal. This corresponds to the period of the Allen treatment with low carbohydrate, protein and fat intake.

Diabetes a Unity Disease.—The brilliant work of F. G. Banting and his co-workers, in isolating insulin as the active principle of the islands of Langerhans, has solved all the mystery in regard to the true cause of

diabetes. Their work, without doubt, has established the unity of all cases of diabetes. The disease, without question, is in all cases dependent upon the failure of these islands to produce their normal internal secretion, whether this be due to a functional or organic disease. Deprive the body of this secretion which is necessary to the proper combustion of glucose, and we get hyperglycemia with all its harmful effects.

Many agencies within the body no doubt play a part in influencing the production of the hormone of the islands of Langerhans. Such an influence, without question, is exerted by the hormones of some of the other endocrine glands through their "accelerator" or inhibitory action. This co-relationship of the action of the hormones of the various ductless glands led von Noorden to construct a few years ago a very elaborate and complicated theory of the etiology of diabetes. To indicate that such an influence is exerted, we have only to recall the fact that carbohydrate metabolism is markedly disturbed in certain diseases of the pituitary, thyroid, and adrenals. The discovery of insulin is likely to prove an active field for future investigations of the effect of the hormones of these glands on that of the islands of Langerhans.

Pathology.—The etiology and pathology are so closely related that it is almost impossible to discuss one without the other. The organic lesions of the *pancreas* which are so important in the etiology of diabetes have been discussed. The changes not already mentioned and particularly those which are regarded as the result of the disease will now be briefly considered.

The *blood* always shows a hyperglycemia. The specific gravity may be increased or diminished, according to the water content. In cases with marked polyuria, in which the watery constituents of the blood are depleted, the red cells may be 6,000,000 per cmm. or more. The latter react differently from those of normal blood with certain aniline dyes, such as with congo-red as demonstrated by Bremer, as well as with eosin and methylene blue. The leukocytes are usually normal in number, or increased only in proportion to the concentration. The writer has observed a leukocytosis of from 18,000 to 25,000 in diabetic coma. The leukocytes contain glycogen. The alkalinity is reduced, particularly in coma. This is occasioned by the utilization of sodium and potassium, and in severe cases of coma, of calcium and magnesium, for neutralizing the β-oxybutyric and aceto-acetic acids. Acetonemia may occur. *Lipemia* occurs much more commonly in severe diabetes than is generally supposed. The fat may be detected in the form of numerous minute dancing granules in the serum in thick preparations of fresh blood. The separated serum has a decided milky appearance. Bloor found that the average amount of total lipoids in the whole blood of normal individuals was 0.59 per cent. His average in 55 cases of severe diabetes was 1.41 per cent. In one of these cases a percentage of 13.1 was found even on a diet of restricted fat and after fasting fourteen hours. Others have recorded very high values, Fraser 16.44 per cent., Fischer 18.12 per cent. and Klemperer 26 per cent. Undoubtedly the chief cause of the lipemia is concerned with the inability of the severe diabetic to burn glucose. As already noted, fat can only be burnt when there is a coincident combus-

tion of a certain amount of carbohydrate. The fat droplets of the blood can be stained with Sudan III and osmic acid. Exudate into the serous sacs may be turbid with lipoids.

No characteristic changes are to be found in the *gastro-intestinal tract.* Frerichs frequently found a thick layer of a fungous growth in the mucous membrane of the fauces and œsophagus. Occasionally the stomach has been found dilated. Swelling, redness, and ecchymoses of the gastric mucosa, have been noted. Tuberculous ulceration of the intestine may occur when there is a pulmonary tuberculosis. A very intractable symptom in rare instances and one of serious prognostic import is an obstinate diarrhœa.

The *cardiovascular system* is very frequently involved in elderly diabetics. The observations of Janeway and Joslin seem to show that diabetes in young individuals is not accompanied by any increase in blood-pressure. In elderly diabetics, however, arteriosclerotic changes are quite common, although there is no conclusive proof that this is dependent on the diabetic condition. Myocardial dilatation and symptoms of myocardial insufficiency are comparatively frequently seen in diabetics after fifty years of age. They are dependent as a rule, upon associated arterial and renal degeneration.

Of the *pulmonary* lesions, tuberculosis is probably the most common. The tissues of the diabetic seem to furnish a specially good medium for the growth of the tubercle bacillus. In the Johns Hopkins Hospital series of 1025 cases there were 38 cases of clinical pulmonary tuberculosis or 3.7 per cent. Acute bronchopneumonia and lobar pneumonia may occur, and either may terminate in gangrene. The writer has seen one case of bronchopneumonia terminate in abscess formation. Grohe, Kuhne, and Ehrlich have shown the cells of the pneumonic exudate to be rich in glycogen. A chronic non-tuberculous interstitial pneumonia has been described. So-called fatty emboli of the pulmonary arteries occur in coma.

The *liver* is usually somewhat enlarged, and fatty degeneration is common. The form of cirrhosis designated by Hanot as *cirrhose pigmentaire diabétique*, which is one of the lesions of hemochromatosis in which diabetes may develop as a late manifestation, has already been described. Poverty of the liver in glycogen is a striking feature. The *pancreatic* lesions have been described. Pancreatic calculi or gall-stones pressing on the duct of Wirsung occasionally occur. They lead to secondary sclerotic changes in the pancreas and produce the most typical form of pancreatic diabetes. There are no changes in the gland that are regarded as secondary to the disease.

The *kidneys* are often enlarged. The most characteristic change is a hyaline degeneration of the epithelial cells of Henle's loop, described by Armanni and sometimes spoken of as the lesion of Armanni. The affected cells present a swollen, transparent appearance, as if transformed into large hyaline vesicles. The nuclei stain well and are pushed to the periphery. Cantanni and others have confirmed Armanni's observations. Ehrlich and Frerichs have described a glycogenic degeneration of the same cells as are involved in Armanni's lesion. The degeneration can

be demonstrated macroscopically by treating the kidney section with Lugol's solution, the affected portion taking on a red color. Straus holds that the hyaline changes described by Armanni and the glycogenic changes described by Ehrlich and Frerichs, are really of the same nature. In some cases he has demonstrated the hyaline changes without finding glycogen present. In such cases, he thinks that the glycogen has been present at one time, but has disappeared before death, leaving only the hyaline changes. Ebstein described a necrosis of the renal epithelial cells, similar to the coagulation necrosis of Weigert in other diseases. Interstitial and parenchymatous nephritis may occur, but there is no reason to believe that diabetes is the cause of the nephritis in these cases. A *cystitis* occasionally occurs. It has been attributed to irritation by the saccharine urine, but it is more likely due to bacterial infection.

Of the lesions of the *nervous system* not already described, Saundby states that congestion and œdema, and thickening of the membranes of the brain, may occur. Williamson, Sandmeyer, and Kalmus have described a degeneration of the posterior columns of the cord similar to the sclerosis of these tracts in tabes dorsalis. Williamson states that the lesion is best seen with the naked eye, when the affected portions appear much paler than does the healthy white matter. These changes are attributed to the action of some toxic agent. The peripheral nerves, particularly those of the lower extremities, may be the seat of an interstitial inflammation, with secondary degeneration of the axis cylinders of the nerve fibres. This *neuritis* may cause clinical symptoms.

Symptoms.—Various writers have been disposed to recognize certain clinical types and thus *acute* and *chronic* cases are described. The acute cases generally occur in children and young adults, the emaciation being marked and the course very rapid. The chronic cases, usually occur in persons who develop the disease after the fortieth year, and in middle-aged and elderly obese individuals. The acute cases, however, may occur in the aged. Osler reported a man aged seventy-three years in whom the entire course of the disease was less than three weeks.

There are the *mild* and the *severe* cases. According to Naunyn, if the glucose disappears with the patient on a non-carbohydrate diet, the case belongs to the former type. If, on the other hand, he continues to excrete glucose, the case is a severe one, for it means that sugar is being produced from the body proteins. The presence of a high ammonia secretion, low respiratory quotient, low CO_2 combining power of the blood, and of β-oxybutyric acid and its derivatives, acetone and diacetic acid, is also indication of a severe type. Further we have the *fat* or lipogenous (diabéte gras) and the *emaciated* (diabéte maigre) cases. We have also the *neurotic* cases due to injuries or functional disorders of the nervous system. There is no fundamental difference in any of these cases, and no satisfactory classification, along the lines indicated, seems possible.

Although the disease is usually accompanied by a certain group of symptoms which especially characterize it, and which may be so abrupt in their onset that the patient can state the date of their appearance with considerable accuracy, yet these may for a long time remain in abeyance, and may even never become a prominent feature. Thus the

polyuria, thirst, increased appetite, emaciation, and weakness, may not be sufficiently marked to attract the patient's attention. The first intimation of there being anything wrong may be a failure in vision. On the other hand, the patient may consult the family physician for an obstinate general or localized pruritus as the first symptom. Similarly, a furunculosis, a severe neuralgia, or impotence, may cause the patient to seek advice. Occasionally general weakness, nervousness, slight change in temperament, mental hebetude, and inability to apply himself to business, may antedate the characteristic symptoms. Too often, unfortunately, the disease gets a firm foothold and has seriously impaired the general health before it is finally recognized.

Polyuria is the symptom most frequently first complained of by the diabetic. In the acute cases, the patient asserts positively that the quantity of urine suddenly became greater, and that he is obliged to get up frequently at night to pass urine. The increase in the quantity of urine is referable to the hyperglycemia. Owing to the increased quantity of glucose in the blood, the latter becomes hyperisotonic, and the fluids of the tissues are absorbed into the circulation more rapidly than in the normal individual, and consequently more water is secreted by the kidneys. The amount of urine may reach 10 to 20 liters daily in the severest cases, although it is rare to see cases in which more than 10 liters are voided in the twenty-four hours. The amount usually bears direct relationship to the percentage of sugar excreted. In certain cases there may be no increase in the urine when glycosuria is present.

Thirst, or polydipsia, may be extreme, and may be complained of as early as, but more often very soon after, the polyuria. It is indirectly traceable to the hyperglycemia, and directly to the desiccation of the tissues already described. It bears a definite relationship to the polyuria.

Increased appetite (bulimia or polyphagia) is a frequent symptom, particularly in the very acute cases. In the milder forms, and in the advanced stages of the severe type, this symptom may be wanting. There may even be loss of desire for food. Notwithstanding the enormous amount of food eaten, progressive emaciation is the rule, especially in the young individual. The increased appetite and the emaciation are largely dependent upon the same causes—the failure of the diabetic organism fully to utilize the carbohydrates of the food. The nutritive changes in diabetes are interesting and deserve some consideration. An individual doing light work requires about 40 calories for each kilo body weight daily, although the work of Chittenden seems to indicate that this is too high. Thus a person of average weight would require 2400 calories for his nutritive needs. Let us suppose this individual to be suffering from diabetes and to be taking a mixed diet including proteins, fats, and carbohydrates, in the following proportions: 160 gm. of albumin, yielding 656 calories; 110 gm. of fat, yielding 1023 calories; and 240 gm. of carbohydrates, yielding 984 calories. This diet provides a total of 2663 heat units, or 263 more than would be required by the individual were he perfectly healthy. Let us suppose that he is excreting 140 gm. of sugar daily. He would therefore lose each day nutritive material to the value of $140 \times 4.1 = 574$ calories. The food of this diabetic consequently

would have the value of only 2663 − 574 = 2089, a deficit of 311 calories. To meet the requirements of energy and heat production, the body must have consumed of its own substance to the value of 311 calories. The tissues drawn on for fuel material to make up for this caloric deficit are the albumins and fats. By estimating the amount of nitrogen in the food and in the urine and feces, it is possible to determine the exact proportion of body-fat and albumin consumed daily to make up for the caloric loss resulting from the failure of the organism to utilize all the ingested carbohydrates owing to a considerable quantity being eliminated in the urine as glucose. This consumption of his own body-fat and albumin necessarily occasions a progressive loss in weight, and the hypothetical case illustrates how the emaciation is brought about. The latter will continue unless the diet is so regulated as to prevent a loss of sugar in the urine. Von Noorden explains the polyphagia in the following way: "The 'stomach hunger' is momentarily stilled, but quickly returns, for 'tissue hunger' is not satisfied. The inordinate appetite of the diabetic disappears only when the useless carbohydrates are cut off and their place supplied by albumin and fat."

The face is often of a deep red color. The skin of the entire body in the majority of cases is dry and harsh. This is due to the fact that the sweat, as is the case with nearly all the secretions, with the exception of the urine, is diminished in amount. The skin may be moist, however. In cases complicated by pulmonary tuberculosis, sweats may occur, and they have been known to alternate with polyuria. The nails are often brittle, and paronychia is not uncommon. There may be some irritability of temper. There is a strong tendency for the individual to become morose or even hypochrondriacal. Some complain of extreme drowsiness during working hours. The temperature in uncomplicated cases is usually subnormal. The pulse is generally increased in frequency, with the pulse-tension normal, excepting in elderly patients in whom the disease is complicated by arteriosclerosis. Joslin has laid emphasis on the increased pulse frequency and attributed it to increased protein metabolism.

The mouth is dry, due to the thirst and to the diminished salivary secretion. The saliva is less alkaline than in health, and that collected from Steno's duct is usually acid in reaction. Frerichs, von Noorden, and Mosler found the saliva almost without exception free from sugar. Frerichs demonstrated sugar in 1 out of 9 cases. The tongue is usually dry and red, and often has a glossy appearance resembling that in psoriasis linguæ. The digestion, notwithstanding the enormous quantities of food taken, is, as a rule, good. Obstinate constipation is the rule. Intractable diarrhœa occasionally occurs. The eyesight, owing to the ocular complications, is often defective. Pain in the lumbar region is often an annoying symptom even early in the disease. Cramps in the calves of the legs occasionally cause much discomfort. Owing the the lowered vitality of the tissues, and owing to the latter being richer in sugar than normally and consequently being a better nutritive medium for the growth of organisms, wounds heal less readily and are much more liable to become infected. In patients with secondary lesions of the cord or peripheral nerves of the lower extremities a sensation of a "giving away" of the knees

may be complained of. This occasionally occurs, however, even without nervous manifestations.

Loss of sexual desire and power in men is common, and may be an early feature. It may reach the grade of actual impotence. Sexual power may return, according to Seegen, with improvement in the patient's other symptoms while under treatment. Occasionally increased sexual desire with power persists throughout the disease. In severe cases of diabetes in women the sexual desire is much impaired, but in mild cases in elderly women it is said to be often increased Amenorrhœa is not uncommon, and may occur early in the disease.

The Urine.—The amount has been considered under polyuria. It is usually extremely pale and clear. The quantity and pallor generally bear a direct relationship to the percentage of sugar present. Occasionally one sees diabetic urine of quite deep color. In these cases there is little or no polyuria. It often has a suggestive greenish tint, and may, when shaken, have a syrupy consistency. It has a sweet taste, and in severe cases with threatening coma, may have a sweetish, fruity odor, owing to the presence of acetone. The specific gravity usually ranges between 1.025 and 1.045. A pale urine with a specific gravity above 1.025 should always lead one to suspect the presence of sugar. In rare instances diabetic urine with sugar demonstrable may have a specific gravity of 1.015 or even lower. A specific gravity above 1.050 is rare. Naunyn has seen a case with 1.060. The highest specific gravity recorded was in 2 cases reported by Bouchardat and Prout, in each of which it was 1.074. Very high specific gravity—1.070 or over—always suggests fraud.

The most characteristic feature is the presence of sugar and the diagnosis is largely dependent upon this. This is almost invariably grape-sugar (glucose, dextrose). Normal urine contains glucose in quantities not demonstrable by the ordinary tests. In rare instances levulosuria may occur either with glucosuria or alone. Kulz and Vogel frequently noted pentosuria in human diabetes, and in experimental diabetes in animals, even after prolonged fasting, showing that the pentose originates in the animal body. The amount of sugar excreted varies considerably at different periods of the day. The period of minimum output is in the late night or early morning hours. According to Naunyn there are two periods of maximum output; one in the late morning hours, the other about six o'clock in the afternoon, occasionally lasting until midnight. The amount of sugar usually begins to increase about one and a half to two hours after a meal. The percentage of sugar should be determined from a sample of urine taken from the mixed twenty-four-hour amount. Knowing the total amount of urine, it is then easy to calculate the total amount of sugar, in grams or grains, excreted daily. This is the only satisfactory way of following the progress from day to day or from week to week. Variations in the percentage of glucose excreted at different periods of the day are much less marked in the severe than in the mild cases, and in the former, the sugar of the night urine may exceed that of the day. In the latter, the variations are often quite marked and the urine of the early morning hours may be free from sugar. The percentage of glucose varies greatly. In the majority of cases it ranges about 3 per

cent. In the severe cases it reaches 5 per cent. or over. It is very rare to meet with more than 8 or 9 per cent., although Naunyn reported a case with 11 per cent. and Higgins and Ogden a case of traumatic diabetes with 20 per cent. of glucose. The total output of sugar for the twenty-four hours may be only a few grams in the mild cases. In some cases the quantity of sugar may be enormous. It is not unusual to see cases with a daily excretion of 500 gm. (16 ounces). Charcot reported a case with 1100 gm. (35 ounces), Lecorhé a case with 1200 gm. (40 ounces), and Dickson a case cited by Naunyn with the enormous output of 1500 gm. (50 ounces).

Many factors influence the sugar output. Diet is the most important one. Carbohydrates cause a marked increase, whereas a diet consisting exclusively of proteins and fat will cause the sugar to disappear in mild cases and, a 5 per cent. green vegetable or starvation diet will often also render the urine free from sugar even in the severest cases. Acute febrile diseases and septic infections often cause a marked reduction. It is not unusual in diabetes with pulmonary tuberculosis accompanied by high fever, to see the sugar almost entirely disappear in the terminal stages. The onset of coma manifestations is not infrequently attended by a marked reduction in the sugar excretion.

The reader is referred to the works on Clinical Diagnosis for the methods of performing the tests for glucose. Those generally used are the Fehling copper test or Benedict's test and the bismuth, fermentation, polariscope, and phenylhydrazin tests. Glucose reduces alkaline copper and bismuth solutions, ferments with yeast, is dextrorotatory, and with phenylhydrazin produces an osazone, the crystals of which melt at 204° to 205° C.

Precautions to Observe in Performing the Sugar Tests.—It is a safe rule never to rely on one qualitative test alone. The most reliable single test is the fermentation test. If there is a rapid reduction of the copper sulphate in performing Fehling's test, one can be reasonably certain that the reducing agent is glucose. Where it is slow and slight, and, especially, if the precipitate be yellow rather than red, other reducing agents must be considered and eliminated. The other substances that reduce alkaline copper sulphate solutions are conjugated glycuronic acid, sometimes eliminated after the taking of certain drugs, alkapton (homogentisic acid), lactose, excess of uric acid, and creatinin. The conjugate glycuronic acid also reduces bismuth, but is differentiated from glucose by being levorotatory as voided, becoming dextrorotatory when the glycuronic acid is split off by boiling with an acid. It does not ferment. Alkaptonuric urine is recognized by being negative with the bismuth, fermentation, and polariscope tests. Its special feature is its darkening on exposure to the air and on the addition of an alkali. Lactose, which is frequently eliminated in the urine in the early days of lactation, and when there is retention of milk in the breasts, reduces copper sulphate and bismuth, and is dextrorotatory, but does not ferment. Pentose reduces copper solutions only after considerable heating and then suddenly throughout the whole fluid. It yields a gray precipitate with Nylander's bismuth test; does not ferment; and may be dextro-

rotatory or inactive, depending upon the variety present. It gives the orcin test. Although excesses of uric acid and creatinin may cause slight reductions of copper sulphate, there should be no difficulty in differentiating these from glucose if one takes the precaution to use one or more of the other tests, with which they are negative.

Other Urinary Ingredients in Diabetes.—*Glycuronic acid*, like sugar, is present in normal urine in minute traces, and is increased in diabetes. It is regarded as one of the intermediary products of carbohydrate metabolism. It is recognized by the orcin test. Rosin and Alfthan demonstrated that the benzyol esters are also increased. These normally do not exceed 2 to 3 gm. daily. Edsall found as high as 12.5 and 13.8 gm. in 3 cases of diabetes.

The urine of diabetics before and during coma symptoms very frequently, if not always, contains β-oxybutyric acid ($C_4H_8O_3$) and its derivatives, *diacetic acid* ($C_4H_6O_3$) and *acetone* (C_3H_6O). Acetone first makes its appearance, later diacetic acid, and still later in the severest cases, β-oxybutyric acid. In a diabetic case it is fully as important for the physician to test for these as for sugar. Their early recognition will aid in so directing the treatment that threatened coma may be warded off. It is not customary to test for *β-oxybutyric acid* as a routine owing to there being no simple, quick test. It is levorotatory and may partly neutralize the dextrorotatory action of glucose. Diacetic acid and acetone should be tested for as a routine. Their presence in the urine always indicates that β-oxybutyric acid is being formed.

Diacetic acid is formed from β-oxybutyric acid by the latter taking on an atom of oxygen and splitting up into diacetic acid and water. It is recognized by Gerhardt's ferric chloride test.

Acetone, when present in large quantities, may give the urine a fruity odor. It may be recognized by Legal's sodium nitroprusside test, or by Lieben's iodoform test.

The *nitrogen* output is greatly increased, chiefly in the form of urea. This is due largely to the greater amount of proteins ingested, but also in part to increased destruction of the body proteins in the more severe cases. Pettenkofer and Voit have shown that, even when fasting, a diabetic patient excreted about 8 per cent. more urea than a healthy person. Leo has shown that the addition of carbohydrates to the diet of a diabetic will occasionally diminish nitrogenous metabolism.

An interesting feature is the extraordinary increase in the *ammonia* nitrogen output in the severe cases, particularly when coma supervenes. According to Neubauer, the average amount of ammonia nitrogen excreted in the urine by a normal individual on a mixed diet is about 0.7 gm. daily. Part of the ammonia which should go to form urea is utilized in neutralizing the acids producing the acid intoxication. Naunyn reports having found an excretion of 5.8 gm. of ammonia in a child weighing 48 pounds, and states that a daily excretion of 6 to 7 gm. is not unusual in adult diabetics. Stadelmann records a case with an elimination of 11 gm. The amount of ammonia excretion can be taken as a safe measure of the grade of acid intoxication in diabetes.

The *uric acid* excretion is usually increased. Gaethgens, in a diabetic

with fever, found the uric acid excretion was 2.2 gm. in the twenty-four hours. The increase is explained by the excessive nucleoproteins taken. It is very common to see diabetic urines with uric acid sediments. This precipitation is probably in part due to the diminished power of diabetic urine to retain uric acid in solution. Bischofswerder has shown that the total *alloxuric bodies* are also increased. Senator found the creatinin increased up to 2 gm. daily. This is referable to the increased ingestion of meat and to the increased destruction of the muscular tissues of the body.

Oxaluria often occurs, with an actual increase in the excretion of calcium oxalate. Teubaum has shown that the lime salts are markedly increased in severe cases of diabetes, but not in the mild. The *sodium chloride* is increased. The *sulphates* and *phosphates* are in excess, owing to the increased destruction of ingested and body protein, with oxidation of the sulphur and phosphorus of the protein molecule. A form of "phosphatic diabetes" has been described by Tessier, Ralfe, and others, due to an excessive excretion of calcium phosphate. There is nervous irritability, deranged digestion, emaciation, and pain in the back. In severe cases there may be polyuria, and the symptoms may simulate diabetes. The affection has really nothing to do with true diabetes, although it is said that traces of sugar have been found in some cases or have subsequently developed.

Albuminuria is absent in the majority of cases of diabetes when they are first admitted to a general hospital. In private practice, with a larger proportion of mild diabetes in elderly persons, it is more common. Five groups of cases of albuminuria may be recognized: (1) Cases of severe diabetes of considerable duration, with traces of albumin, but no other evidence of nephritis. (2) Those in diabetics of advanced age, with indications of arterial changes. (3) Those in which there are definite evidences of chronic nephritis, such as œdema, headaches, retinitis, and cardiovascular changes. (4) Cases of severe diabetes with diabetic coma. When coma symptoms definitely manifest themselves, albuminuria is practically always present. (5) Cases in which albuminuria is due to a cystitis, or a balanitis in the male and vulvitis in the female. Naunyn and others state that diabetes mellitus occasionally passes over into a true nephritis, with disappearance of the glycosuria.

Casts are rare in diabetic urine except in cases complicated by actual nephritis. There is one striking exception, however. Külz first pointed out that diabetic coma is accompanied by an abundant deposit of casts. A urine previously free from them and quite clear may suddenly become turbid, even on voiding, owing to the enormous number of casts present. These settle to the very bottom of the glass as a grayish-white sediment. Microscopically, the field is found to be crowded with rather short hyaline and granular casts. The albuminuria and cylindruria of diabetic coma are probably evidences of a toxic nephritis. In cases of cystitis, balanitis, and vulvitis, pus cells are found in the urinary sediment.

Diabetic urine, on standing, soon becomes turbid, owing to the growth of yeast cells. This fact is of practical importance, as it indicates that suspected urine should be examined qualitatively and quantitatively as

soon as possible after being voided, particularly in warm weather. The yeast causes fermentation of the sugar, and when the glycosuria is slight, it may cause a complete disappearance of the glucose, and in all cases will cause a reduction in the percentage of sugar. The presence of yeast cells in urine should always arouse a suspicion of the existence of glucose. In balanitis in the male and vulvitis in the female, there is often a fungus growth in the inflamed mucous surfaces, and fungus spores and mycelia may be washed away in the urine during voiding.

Occasionally yeast cells and fungi develop in the bladder and set up fermentation processes, with the production of gas, *pneumaturia*. This is a rare condition. Leube found that diabetic urine contains a substance which gives all the reactions of *glycogen*. *Lipuria* has been described, the fat occurring in the form of a fine emulsion.

Complications.—1. **The Skin.**—*Boils* and *carbuncles* are fairly common, so much so that when they exist one immediately thinks of diabetes as a cause. There were 7 cases of furunculosis and 3 with carbuncles in our series of 1025 cases. Their frequency is due to the susceptibility of the tissues of the diabetic to infection. Boils are more common in the milder forms of the disease and in stout diabetics. The commonest seats are the neck, back, and buttocks. Cultures usually show staphylococci. Carbuncles are less common but more serious. They are more likely to occur in the severe cases and may precipitate coma.

Owing to the irritation of the genitals by the saccharine urine, and to the growth of fungi (hyphomycetes) in the skin, inflammation of the prepuce and glans in the male, and vulvitis in the female, may occur. This may be attended by intolerable *pruritus*, particularly in women, in whom local boils or phlegmons of the genitals may develop. The *general pruritus* of diabetes is due in all probability to irritation of the sensory nerves by the sugar in the blood, just as pruritus in jaundice and uremia is due to circulating toxins. *Urticaria*, *purpura simplex*, *purpura hemorrhagica*, *dermatitis herpetiformis*, *gangrena diabetica*, *bullosa serpiginosa* (Kaposi) may occur. Œdema of the feet, even without evident renal or cardiac affections, is not uncommon in advanced cachectic cases. A curious mottled cyanosis of the extremities is sometimes observed. In rare instances, the skin may be bronzed, constituting the so-called *diabète bronzé cases*, hemochromatosis, in which glycosuria sometimes occurs in the late stages when the interstitial pancreatitis becomes marked. *Herpes zoster* and *perforating ulcer* of the foot occasionally occur, and are expressions of a diabetic neuritis. There were 14 cases of perforating ulcer of the foot among the 1025 cases. The frequency has been diminishing in recent years. A *paronychia diabetica* may occur and result in the loss of the nails. Williamson observed 3 cases with bulbous fingers, due apparently to vasomotor changes. The writer has seen 3 cases of Dupuytren's contraction of the palmar fascia in three diabetic brothers. There were 3 cases in our series of 1025 diabetics.

The diabetic is very susceptible to local pyogenic infections. In our series there were 19 cases with *cellulitis* and *abscess formation*. In 5 there was osteomyelitis of the bones of the feet.

Diabetic gangrene occurs usually in diabetics after fifty. The glycosuria is usually of a mild grade It is commonest in the lower extremities, and generally begins with a bluish discoloration and then a blackening of the skin of the big or little toe. It is of a moist type and may subside, but usually extends gradually to involve the whole foot or leg until stopped by amputation. It may start in the heel. It occurred in 49 of our 1025 cases. William Hunt analyzed 64 cases. In 50 the distribution was as follows: feet and legs, 37; thigh and buttock, 2; nape of the neck, 2; external genitals, 1; lungs, 3; fingers, 3; back, 1; eyes, 1. The artery supplying the affected area shows arteriosclerosis in the vast majority of cases. In many instances it is thrombosed, and Naunyn stated that he never failed to find obliteration of the pulse in the early stages of the complication. *Thrombophlebitis*, particularly of the veins of the lower extremities, occasionally occurs. It was present in 5 in our series. Œdema is not uncommon. It is increased by the administration of sodium bicarbonate or high salt intake but usually disappears rapidly on their withdrawal.

Xanthoma diabeticorum occurs as a very rare complication. The lesions consist of small nodules about the size of a pea, and having a yellowish or yellowish-red color. They are slightly sensitive and occur mainly on the buttocks, forearms, knees and palms of the hands. The eyelids are much less likely to be involved than in the xanthoma multiplex accompanying chronic jaundice. The xanthomata appear rapidly and disappear quickly with relief of the lipemia by diabetic treatment. In 1 of our cases the xanthomata on the arms and legs reached 2 cm. in diameter. Some were ulcerated. They disappeared rapidly under insulin treatment with the clearing up of the lipemia. They may recur several times. There were 4 cases in our series. In 1924, Major collected 74 cases from the literature, in addition to reporting 3 of his own. The nodules contain cholesterol. His cases all showed lipemia and cholesterol esteremia, and the nodules are dependent on this condition rather than on the glycosuria.

2. **Gastro-intestinal.**—An aphthous stomatitis due to the oïdium albicans occasionally occurs. At autopsy the pharynx and œsophagus often show a diffuse growth of this fungus. Gingivitis with pyorrhœa alveolaris frequently develops. The teeth decay rapidly and tend to loosen and fall out owing to the pyorrhœa. Gastrectasis occasionally results from the enormous quantities of food and liquids taken. There may be actual gastric catarrh. Although moderate constipation is the rule, one occasionally meets with a case of obstinate diarrhœa. This is referable to an intestinal catarrh. Steatorrhœa, or fatty stools, may occur in pancreatic diabetes. Here fat digestion is interfered with, owing to changes in the pancreatic secretion, and the stools are of a pulpy consistence, of a dirty, dark-gray color, and of a greasy appearance. In these cases the movements are often very bulky, and at the end of defecation as much as a tablespoonful of almost pure fat may be passed. In a patient seen with A. D. Atkinson, of Baltimore, the autopsy revealed the presence of a large pancreatic calculus. Microscopically, large oil-globules and abundance of fatty acid and soap crystals are seen.

3. **Pulmonary.**—One of the commonest is *pulmonary tuberculosis.* Clinical tuberculosis was found in 38 of our cases. Griesinger analyzed 250 cases of diabetes, and found pulmonary tuberculosis in 42 per cent., and to be the cause of death in 39 per cent. In 50 autopsies, Frerichs found the lungs tuberculous in 25. In 149 of Naunyn's "pure" diabetic cases, it was present in 25, or 17 per cent., while in 113 cases, due to evident organic disease, there were 8, or 7 per cent. With the progress of the tuberculous process the glycosuria often diminishes or may entirely disappear. Death may result from acute *pneumonia*, either lobar or lobular. A chronic interstitial pneumonia may occur. The pneumonia may be complicated by abscess of the lung. Gangrene of the lung is not very uncommon. Naunyn saw 12 cases, all of which terminated fatally with one exception. He describes three forms—an acute, a subacute or chronic, and a form with numerous gangrenous foci complicating a chronic pneumonic process, with fibrous induration.

4. **Heart and Arteries.**—Sufficient importance has not been attached to myocardial insufficiency in diabetes. It is not rare and occurs chiefly n the obese cases and in those with arteriosclerosis. The blood-pressure is usually moderately increased. The arterial changes may cause intermittent claudication, as was first pointed out by Charcot.

5. **Renal.**—These have been sufficiently discussed.

6. **Nervous System.** Here only the nervous features directly referable to the diabetes will be considered.

(*a*) *Peripheral Neuritis.*—This is the commonest nerve complication and occurred in 27 cases in our series. The numbness, tingling, cramps, and neuralgias are probably expressions of a mild neuritis. Sciatica is not uncommon, and other peripheral nerves, such as the inferior dental, may be affected. The neuritis may be multiple. Thus both ulnar nerves may be involved, causing muscular paralysis and anesthesia of the skin. As expressions of the neuritis, must be mentioned *falling out of the nails*, *glossy fingers*, *herpes zoster*, and *perforating ulcer of the foot.* The perforating ulcer closely resembles that of tabes. Williamson met 4 out of 140 cases. There were 14 among our 1025 cases. The sole of the foot, in the region of the metatarsophalangeal joint, is the commonest seat. The bone may be exposed or the joint opened. A corn may precede the ulcer. Attempts to remove the corn lead to infection, and the ulcer proceeds. On the other hand, trophic changes, due to the neuritis, constitute the chief etiological factor, and the ulcer may commence with superficial death of the skin. The ulceration is often painless. As the knee-jerks are often absent, the lesion may be mistaken for the perforating ulcer of tabes unless the urine is examined.

A so-called *diabetic tabes*, resulting from a polyneuritis, has been described. The pseudotabes closely resembles true tabes dorsalis, and was first described by Fischer, in 1886. It is characterized by lightning pains in the legs, loss of knee-jerks, and loss of power of the extensors of the feet. There is a characteristic *steppage* gait similar to that seen in arsenical, alcoholic, and in other forms of neuritic paralysis. A typical Argyll-Robertson pupil is rarely, if ever, present, although Charcot states that there may be atrophy of the optic nerve.

(*b*) A *diabetic paraplegia*, probably due to a peripheral neuritis, with paralysis of the arms and legs, has been described.

(*c*) Degeneration of the posterior columns has been described by Williamson, Sandmeyer, and Kalmus.

(*d*) *Hemiplegia* occasionally occurs. This, no doubt, is practically always due to cerebral vascular disease. Cases have been reported in which careful search has failed to reveal evidences of hemorrhage, thrombosis, or embolism. These have been attributed to some toxic origin, but such an opinion must be accepted with considerable reservation.

(*e*) *Reflexes.*—The knee-jerks are often absent, first pointed out by Bouchard. Statistics differ as to the frequency with which the knee-jerks disappear. Grübe found them absent in 13.5 per cent. of his cases; Williamson found them absent in 50 per cent. Their disappearance is probably dependent on a peripheral neuritis or changes in the posterior columns of the cord. The Achilles reflex may disappear before the patellar. The superficial reflexes—plantar and abdominal—are present in practically all cases. A patellar reflex may return after being lost. The condition of the reflexes bears no definite relationship to the prognosis, although the knee-jerks are more likely to be found absent in hospital than in private practice, the former cases being usually more severe.

(*f*) *Mental Complications.*—In addition to the psychical symptoms already described, a group of mental symptoms is occasionally met with closely resembling *general paresis*. The mental symptom-complex is often improved under antidiabetic treatment.

7. **Special Senses.**—Of the ocular complications, *cataract* is the commonest. There were, however, only 16 cases in our series. Frerichs observed it in 19 cases out of 400 diabetics; Williamson, in 9 out of 100; and Seegen, in 4 per cent. of his cases. It occurs in the young as well as in the old. It is usually bilateral, and, in the young, of the soft variety, but in old diabetic patients, it is indistinguishable from the non-diabetic variety. There is no satisfactory explanation of its cause. The view that it is due to abstraction of water is no longer generally supported. There has been some difference of opinion among ophthalmologists as to whether a true *retinitis* dependent upon the diabetic condition actually occurs. Some consider that it is dependent on the associated vascular or renal lesions. Harry Friedenwald, in a review of the subject in 1925, adheres to the view that a retinitis centralis punctata of diabetic origin actually occurs. Williamson found it in 7 cases among 100 diabetics, but, in some of these, renal disease could not be excluded. It was first described by Jaeger in 1856. Hirschberg describes three types—a retinitis hemorrhagica diabetica, a retinitis centralis punctata, and a combined form. Rarely a *diabetic iritis* with hypopyon occurs. Diabetic amblyopia, due to a central scotoma, and *optic neuritis*, are rare complications. De Schweinitz says that *premature presbyopia*, with failure to accommodate, is a common and often an early symptom. Sudden amaurosis similar to that in uremia may occur. The vitreous may contain masses of cholesterin crystals. Such a case came under the writer's observation. *Lipemia retinalis*, a very remarkable condition, probably occurs more commonly than is generally supposed. It develops only in the severe

cases with lipemia. There were 2 recognized in our series. In 1923, McCann reported one of these and found only 28 cases in the literature. The white retinal vessels stand out conspicuously on a salmon-pink background. Both arteries and veins are involved. The picture may persist for some time after the lipemia has disappeared under insulin or diabetic treatment. This suggested to McCann the idea that the vessels may be surrounded by fat-containing lymph or fat deposited in the adventitia of the vessels, so that the light is abnormally reflected or refracted and that the appearance might depend on the physical states of the fats or lipoids of the blood rather than on the total quantity. *Ear* complications are not common. Furuncles in the external auditory meatus, and acute otitis media occasionally occur.

8. **Reproductive System.**—When diabetes develops during the child-bearing period, amenorrhœa usually results, and it is said that atrophy of the uterus may occur. Conception is rare. According to Gaudard, 33 per cent. of pregnant diabetic women abort. Herman states that premature delivery, due to intra-uterine death of the fetus, has occurred in about two-thirds of the published cases of pregnancy with diabetes. A diabetic mother may bear a healthy child, however, and has never been known to bear a diabetic one. Usually the diabetes becomes aggravated after delivery. Pregnancy may go to full term with marked amelioration or complete disappearance of the diabetic features. Herman favors early delivery, as the chances are two to one that the child will die *in utero*, and the earlier the pregnancy ends the more likely are the diabetic symptoms to ameliorate in the mother.

9. **Diabetic Coma.**—This is the most important and most serious of the complications of diabetes. Three types of coma occur:

(*a*) *Typical dyspnœic coma*, or Kussmaul's "air-hunger" type. This is the form that Kussmaul described, and is by far the most frequent of the three. As premonitory symptoms there may be lassitude, headache, epigastric pain, and occasional vomiting. The patient becomes restless and excited, and tosses about in bed. His speech becomes thick and eventually incoherent. He grows gradually duller, and eventually passes into deep coma. The pulse becomes small in volume, of low tension, and frequent, often reaching to between 120 and 140 per minute. A characteristic form of dyspnœa develops. It is inspiratory at first, but later expiration is also involved. When fully developed the respirations are full and voluminous; they are loud and can be heard a considerable distance, although they are not stertorous as in apoplexy; they are quite regular and are usually not increased in frequency. The volume of the chest is greatly increased with each inspiration, and it is this apparent demand of the system for air that led Kussmaul to designate the phenomenon as "air-hunger." The temperature is usually subnormal. There may be some cyanosis. The breath often has a fruity odor (owing to the exhalation of acetone), which may pervade the whole room. The urine may also have an acetone odor. Traces of albumin and enormous numbers of short hyaline and granular casts occur in the urine just before and during the coma. Before the discovery of insulin death almost invariably resulted within seventy-two hours after the onset of the coma. Frerichs and others recognize also the two following forms:

(*b*) *The So-called Alcoholic Form.*—With headache and symptoms suggesting alcoholic intoxication; the speech becomes thick, the pulse rapid, and, without dyspnœa, coma supervenes; the patient soon dies.

(*c*) *The Diabetic Collapse.*—The patient suddenly begins to suffer from drowsiness and great weakness. The extremities become cold; the hands, feet, and face become livid; the pulse is small, thread-like, and 120 to 130 to the minute. The respirations are slightly quickened, but are shallow and not dyspnœic in character. Drowsiness develops, coma supervenes, and the patient dies in ten to twenty hours. There is no acetone odor to the breath nor acetone or diacetic acid in the urine. The collapse is believed to be due to cardiac failure, probably induced by myocardial changes.

Anomalous forms of coma occur, due to renal disease, cerebral tumor, meningitis, and apoplexy. The coma in these cases is due to the accompanying disease and not to the diabetes. The true diabetic coma of Kussmaul, or the "air-hunger" type, is by all means the most frequent and most important, and the following considerations mainly concern this form. A large percentage of deaths in diabetes are due to coma, and it is almost invariably the cause in children. An idea of its frequency can be gathered from the following statistics: Of Naunyn's 44 fatal cases, 19 died in coma, 12 of which were of the dyspnœic type. Frerichs reported 150 deaths from coma out of a total of 250 fatal cases; Taylor, 26 out of 43; Mackenzie, 19 out of 87; and Williamson, 28 out of 40. Up to December 18, 1915, coma was the cause of death in 66 per cent. of the total deaths in Joslin's cases. Showing the influence of careful treatment, he found that of 33 cases dying in hospitals from April 1, 1919, to July 1, 1923, the percentage of deaths due to coma was 21. In the Johns Hopkins Hospital series of 1025 cases there were 102 deaths and 45 of these or 44.1 per cent. were due to coma.

Certain factors tend to predispose to the development of coma. Among these are constipation, excessive fatigue, the onset of various complications, such as carbuncle and pneumonia, subjection to an operation, and sudden changes in diet.

Diabetic coma or "acidosis," as Naunyn first called it, is due to an acid intoxication owing to an accumulation in the blood of the so-called "ketone" bodies, β-oxybutyric acid and its derivatives, diacetic acid and acetone. It is due to a faulty fat metabolism dependent on the fact that with the increasing severity of the diabetes the diabetic patient eventually may completely lose his ability to burn sugar. Fat is only completely burnt when there is a simultaneous burning of a certain amount of sugar in the carbohydrate furnace. It has been estimated by Magnus-Levy that out of 100 gm. of fat, 36 gm. of β-oxybutyric acid may be produced. It should be remembered that a certain amount of this acid may also be derived from the amino-acids of protein, although the amount derived from this source is very small as compared with that formed from fat. None is derived from carbohydrate. By its action on the respiratory centre it causes the characteristic dyspnœa; and from its effect on the brain in general, coma supervenes. The β-oxybutyric acid is eliminated in the urine not as such, but in combination with the bases, chiefly as

sodium oxybutyrate. In severe cases the output is enormous, reaching to between 100 and 200 gm. daily, and in a case reported by Külz, to 225 gm. Naunyn estimated the amount of β-oxybutyric acid in the tissues of a patient near coma between 200 and 300 gm. Bock, Field and Odair found the total acid in the form of diacetic acid in a patient recovering from coma to be 103 gm. For a considerable time the available bases of the tissues (sodium, potassium, etc.) are sufficient to neutralize the acid; but when it is excreted for long periods these become used up, and then ammonia, which becomes the end-product of protein metabolism instead of urea, is called on for neutralization. This accounts for the enormous output of ammonia, reaching to 7 or 8 gm. in cases of threatened coma. The acetone excretion in the urine may reach 10 gm. or more daily. That an acetonemia exists is indicated by the acetone odor of the breath in some cases. The presence of diacetic acid in the urine in the vast percentage of cases means that β-oxybutyric acid is also present.

The presence of β-oxybutyric acid or diacetic acid in the urine should always serve as a danger-signal of approaching coma. There are exceptions to this rule, however, for one occasionally meets with cases in which a marked diacetic acid reaction persists for months or even years. Naunyn refers to a case in which there was an excretion of 100 gm. of β-oxybutyric acid lasting for months, and of another diabetic in whom it had been detected for years.

The degree of acidosis may be determined by estimating the alkaline reserve capacity (combining power) of the blood for CO_2. Normally, this varies between 55 and 75 volumes per cent., with an average of 65 volumes per cent. In severe acidosis it may fall to 20 or 15 volumes per cent., which, in the pre-insulin days, were practically always fatal levels. The respiratory quotient, which normally is between 0.80 and 0.83, may fall as low as 0.65 to 0.70. The hydrogen-ion concentration—pH—of oxalated normal blood is pH 7.35. In severe diabetic coma and in artificially produced acidosis in dogs it may fall to 7.0 or slightly below. Another measure of the degree of acidosis is the amount of ammonia eliminated in the urine. Normally, from 0.5 to 1.0 gm. is excreted daily. It may reach 7 to 8 gm. in severe acidosis.

As a general rule, the addition of moderate amounts of carbohydrates to the diet causes a diminution in the excretion of acetone, as well as of the β-oxybutyric acid when it is present; their withdrawal causes an increase. While this is the rule in the mild cases, in the severest there are often exceptions. It seems to be quite certain that, when the capacity for oxidation in the body is not too much lowered, the presence of moderate amounts of carbohydrates in the food aids in the oxidation process and protects from destruction the fat which is believed to be the main source of the acetone bodies. The feeding of fats, however seems to be a frequent cause for an increase in these bodies, as has been shown by Schwartz, Joslin and others. The chief object in the treatment of coma is to increase the ability of the diabetic to burn sugar. In the past this has been fairly successful by intelligent dietetic management, thus resting the islands of Langerhans. Since the discovery of insulin this remedy has become the best agent in preventing coma.

With the development of coma manifestations and the appearance of β-oxybutyric acid in the urine, the sugar excretion often markedly diminishes, and the percentage of acid, which rarely reaches beyond 0.5 to 1 per cent., may exceed that of the sugar.

Course and Prognosis.—In children and very young individuals, diabetes runs a very rapid course, and in the pre-insulin period was almost invariably fatal from coma. Since its introduction Howland has lost only 1 case at the Harriet Lane Home for Children. Sufficient time has not yet elapsed to settle the question whether by the use of insulin diabetic children can be carried along to an age when the menace to life is materially lessened. Cases are recorded in young individuals in whom the disease ran its entire course to a fatal termination with five weeks. Generally speaking, the later in life the symptoms first manifest themselves, the better is the prognosis. The majority of cases after middle life run a chronic course, and it is not very uncommon to see stout, elderly individuals in whom the disease has lasted ten to fifteen years. Cases with hereditary influences are the most favorable. Once the disease is well-established, it is seldom, if ever, that a permanent cure is effected. Occasionally, however, one sees a glycosuria persisting for months or years in a very neurotic individual eventually entirely disappear. Naunyn cites cases of acute or subacute diabetes resulting from head-traumas in which there had been a permanent cure. The question arises, are these cases of true diabetes or traumatic glycosuria? It is always well to determine the power of the individual to warehouse carbohydrates. If an individual on a non-carbohydrate diet excretes no sugar, the case may be considered a mild one. If, on the other hand, sugar is excreted, it means that it is being manufactured from the body proteins, and the case is a severe one. The presence of β-oxybutyric acid and diacetic acid in the urine is in the majority of instances of serious import, as they indicate the possibility of approaching coma. Before the days of insulin many threatened coma cases in the pre-coma stage were saved by proper dietetic regulations. Once coma was established very few were rescued no matter what measures were adopted. With insulin therapy the pre-coma cases can now be rescued from the danger zone and the literature is revealing an increasing number of cases that have been saved even after coma has actually supervened.

The number of years added to the life of the diabetic patient has been materially increased by the more intelligent dietetic treatment adopted in the last ten years. This, no doubt, will be materially increased by the more general use of insulin.

The *mortality* of diabetics in hospital practice is naturally high owing to the fact that it is the severer type of cases that seek hospital treatment. Of the 1025 cases admitted to the medical wards of the Johns Hopkins Hospital, 102, or 10 per cent. died. The percentage of deaths, naturally, in private practice is much lower, owing to the fact that more mild cases come under observation.

Diagnosis.—There is usually no difficulty in arriving at a diagnosis if the precaution be taken to use two or three urinary tests, including fermentation, in any doubtful case. The presence of conjugate glycuronic

acid compounds, homogentisic acid (alkaptonuria), pentose, levulose, lactose, excess of uric acid, or creatinin, may cause error. In a few of the cases of alkaptonuria the condition has been mistaken at first for diabetes as in the case reported by the writer. The mistake is due to the fact that the homogentisic acid which is eliminated in the urine reduces alkaline copper sulphate solutions. The characteristic which the urine possesses of darkening on standing or on the addition of an alkali should arouse suspicion. Alkaptonuric urine is negative with the bismuth, phenylhydrazin, fermentation, and polariscope tests.

Deception may be practised and Osler cited a case under his care of a young girl who had a urine with a specific gravity of 1.065, and in which the reactions proved to be those of cane-sugar. The literature records a case in which a woman, after detection, bought cane-sugar and introduced it into her bladder.

Pentosuria is more common than is generally supposed and some of the cases have been mistaken for diabetes. Salkowski and Jastrowitz reported the first case in 1892. The urine contained a copper-reducing substance which was optically inactive, did not ferment, and which from its osazone they identified as pentose. T. Janeway reported 2 cases in brothers and states that there is a family predisposition to the disease. He describes three forms: (1) The alimentary pentosuria, due to the ingestion of large amounts of vegetables or fruits containing pentosanes; (2) rare cases occurring in severe diabetes in which the inability to burn carbohydrates extends to the pentose; (3) chronic pentosuria occurring without reference to the pentoses of the food. The sugar excreted in this form is the optically inactive *r*-arabinose. Pentosuria is recognized as follows: Fehling's solution is reduced in an atypical way, the color remaining unchanged for a minute or so after boiling, and then turning suddenly a greenish yellow or muddy orange color throughout. It gives the phenylhydrazin test, but is optically inactive and does not ferment. If doubt still remains the orcin test must be performed, in which the absorption bands of pentose are found with the spectroscope.

Treatment.—Prophylaxis.—Prophylactic dietetic measures should be undertaken in all families in which the history reveals a predisposition toward diabetes. The members of such families should be warned against the liberal use of carbohydrates. These should be considerably restricted. There is often a tendency to obesity in these families and no one has emphasized more emphatically the importance of overweight as a contributory cause of diabetes than has Joslin. It should be our duty to regulate the diet of these patients so that the weight will gradually reach their ideal weight for their height or be maintained slightly below it. A carbohydrate tolerance test, by the method already described, should be carried out wherever possible in all members of families in which there is a predisposition to diabetes. A lowered tolerance may thus be demonstrated even in the preglycosuric stage. Demonstration of a lowered tolerance should be a warning and lead to a restriction of the carbohydrate intake.

Weight.—The diabetic patient should weigh regularly at least once a week. In hospital cases, where careful metabolic studies are being

made, the weight should be recorded daily. It seems probable, now that we have insulin, that the most satisfactory weight for a diabetic is his ideal weight taking into consideration the height. A fairly accurate measure of this is to allow 110 pounds for 5 feet, and to add 5½ pounds for each additional inch. Since the starvation treatment first recommended by Allen in 1914, and strongly advocated by Joslin, both have strongly urged that the diabetic should be kept considerably below the ideal weight. One gets the impression that this is being urged less strenuously since the introduction of insulin.

Hygienic.—It is very important to look after the personal hygiene. Daily baths assist materially in keeping the skin functions active, and diminish the liability to furunculosis. By personal cleanliness the distressing pruritus can be partially alleviated. To the thin diabetic, with a dry, harsh skin, the luke-warm bath is often soothing. The more robust patients can stand a cold bath. An occasional Turkish bath is useful in the obese cases. Light woollen underwear should be worn. Moderate exercise should be taken, as a certain amount of muscular activity favors sugar combustion. Violent physical exertion should be avoided in the severe cases, as it tends to induce coma. Massage is useful, as it tones up the muscular system and thus probably aids carbohydrate metabolism. All sources of worry and anxiety should be eliminated as much as possible. It is of the utmost importance that constipation should be corrected, as in severe cases it is held by many to favor the development of coma. Patients with corns should be warned against cutting them to the extent of producing bleeding in order to prevent the development of perforating ulcers and local infections. Thorough and regular bathing of the feet will undoubtedly lessen the likelihood of gangrene, notwithstanding the arterial changes and disturbed metabolism back of it.

Dietetic.—The symptoms of diabetes are dependent upon the development of a hyperglycemia due to disease of the islands of Langerhans, and clinically revealed by the occurrence of glycosuria. The object of our treatment, therefore, is to combat this hyperglycemia. The best indication of the success of any line of treatment is the disappearance of sugar from the urine. Dietetically, this is best attained by restriction or complete elimination of carbohydrates from the food. In severe cases it is also often necessary to restrict the proteins, since 58 per cent. of the protein molecule yields glucose. It is also necessary to remember that 10 per cent. of the fat molecule goes to the formation of glucose from the glycerol radicle that is split off.

From the therapy standpoint the profession has seen the management of diabetes pass through various phases. These may be roughly summarized as follows:

1. The period of haphazard, rather unscientific treatment dating from the time when Dobson first recognized the importance of restricting the carbohydrates of diabetics in 1676 down to about 1895.

2. From 1895 to 1914 the influence of the Strassburg School, Naunyn, with Minkowski, von Mering, Magnus-Levy and Weintraud, and later of von Noorden and his co-workers was dominant. This was the period

of low carbohydrate but high protein and fat diets, with occasional "starvation" days, and with the administration of large amounts of alkali to combat the acidosis.

3. With the year 1914 began the period of prolonged fasting and undernutrition recommended by F. M. Allen and strongly advocated and made generally popular through the teaching of Joslin.

4. The year 1920 ushered in a new epoch when Newburgh and Marsh showed that nitrogen equilibrium in the diabetic could be maintained on a very low protein and low starch diet when sufficient calories were provided in fat.

5. The year 1922 marks the date of the introduction of insulin therapy by Banting.

In arranging the diet in diabetes, strictly speaking, no two cases can be treated alike. The individual requirements for each case should be determined. This entails a knowledge of the composition of the various foods and the method of working out their caloric values.[1] The burning of 1 gm. of carbohydrate yields 4 calories, 1 gm. of protein 4 calories, 1 gm. of fat 9 calories, and 1 gm. (1 cc.) of alcohol 7 calories. It is pretty generally agreed that the dietetic requirements of an individual at rest is 25 calories per kilo body weight (1 kilo = 2.2 pounds). In hospital cases, however, it is customary to use either the Du Bois or Harris and Benedict formulas for determining the maintenance requirements of each individual case. The Du Bois method is based upon his formula for calculating the body surface. Having obtained this, it is multiplied by the calories computed by him to be standard for square meter body surface for age and sex.

The Du Bois formula for ascertaining the body surface of men and women is as follows:

$$\text{Area (sq. cm.)} = \text{weight}^{0.425} \times \text{height}^{0.725} \times 71.84.$$

in which the product of the weight in kilograms raised to the power 0.425 and the height in centimeters raised to the power 0.725 is multiplied by the factor 71.84.

The Du Bois table for estimation of the calories per square meter body-surface is as follows:

Age in years.	Males.	Females.	Age in years.	Males.	Females.
14 to 16	46.0	43.0	40 to 50	38.5	36.0
16 to 18	43.0	40.0	50 to 60	37.5	35.0
18 to 20	41.0	38.0	60 to 70	36.5	34.0
20 to 30	39.5	37.0	70 to 80	35.5	33.0
30 to 40	39.5	36.5			

The calculation is as follows: Sex, male; age in years, 24; height in centimeters, 170; weight in kilograms, 63.

$$\text{Area (sq. cm.)} = (\text{weight } 63)^{0.425} \times (\text{height } 170)^{0.725} \times 71.84 = 17.305 \text{ sq. cm.}$$

$$= 1.73 \text{ square meters}$$

$1.73 \times 39.5 = 68.3$ calories per hour.

$68.3 \times 24 = 1639$ calories per 24 hours.

[1] For the composition of the various foods the reader is recommended to consult the following publications.

Atwater and Bryant: *U. S. Department of Agriculture, Bull.* No. 28, 1906.

Locke: "Food Values," New York, 1911.

Street, J. P.: Report of the Connecticut Agriculture Station on Diabetic Foods.

Having determined the maintenance requirements in calories it is a simple procedure to calculate a 10, 20 or 30 per cent. increase or reduction in calories in any individual case. It will be observed that the younger the individual the greater are the calorie requirements.

Until the last few years the dietetic care of the diabetic was largely confined to the determination of the amount of carbohydrates which should be allowed in the food, without paying proper attention to the amount of protein and fat best suited to each individual case. When we realize that the metabolism of protein and fat both yield glucose and fatty acids it will readily be seen how important it is that the amounts of these foodstuffs should also be regulated. Shaffer has emphasized the importance of determining the ketogenic and antiketogenic properties of foods. The ketogenic foods, that is, those capable of producing the ketone bodies, are the fats and proteins. The antiketogenic foods are the carbohydrates. Accepting the axiom that "fats burn in the fire of the carbohydrates," it will readily be seen that in the diabetic the amount of fat allowed should depend upon the number of grams of carbohydrate he is capable of burning. This F. A. : G. (fatty acid to glucose) ratio has been found to vary considerably by various investigators. It has been found as high as 4 : 1, while the urine remained free from acetone bodies. On the other hand Mosenthal found evidences of acidosis with a ratio of 0.74 to 1. Most authorities agree that a ratio of 1.5 : 1 is about the proper one to adopt although Mosenthal puts it at 1.2 : 1.

The following table shows the yield of glucose and fatty acids from proteins, fats and carbohydrates:

100 grams.	Glucose, grams.	Fatty acid, grams.
Protein yield in the body	58	46
Fats yield in the body	10	90
Carbohydrates yield in the body	100	0

Formulæ for determining the F. A : G. ratio have been worked out by Shaffer, Wilder and Woodyatt. Woodyatt, assuming a ratio of 1.5 gm. of fatty acid to 1 gm. glucose, gives three formulæ for the determination of the fat for the quantity of the glucose tolerated:

$$(1)\quad G = C + 0.58\,P + 0.1\,F.$$

The fatty acids are estimated by the following formula:

$$(2)\quad FA = 0.46\,P + 0.9\,F.$$

Assuming that when the ratio $\frac{FA}{G}$ exceeds 1.5, ketonuria develops, the maximum quantity of fat is shown in the following formula:

$$\frac{C + 0.58\,P + 0.1\,F}{0.46\,P + 0.9\,F} = 1.5 = F = 2\,C + 0.54\,P \text{ or simply}$$

$$(3)\quad F = 2\,C + \frac{P}{2}$$

With regard to the amount of protein permissible for the diabetic, all agree that it should be kept low. Certainly not over 1 gm. per kilo body weight and permanently not below 0.66 gm. per kilo according to Joslin.

If the method of determining the caloric requirement of a diabetic by multiplying the weight in kilos by a certain number of calories (25 calories for diabetics at rest or a higher number for those doing moderate work) is adopted, it should be remembered that the calculation should be made from the ideal rather than from the actual weight.

Mild, Moderately Severe and Severe Diabetes.—In the past it has been customary to adopt the above classification from the standpoint of therapy. Diabetes in children is always severe, whereas beyond fifty years of age the tendency is for the disease to be mild. The existence of acidosis indicates a severe type. There is a tendency to abandon the classification based on the patient's ability to warehouse carbohydrates, since so many other factors enter into the situation.

In the dietetic management the physician must use his judgment and experience in deciding whether the patient should have hospital management or whether home treatment is advisable. There is no question but that all diabetics would be benefited by hospitalization. Their lives would be prolonged and the risks of complications greatly lessened. Every patient should be taught the principles of regulating his diet and also how to examine the urine for sugar with Benedict's solution.

One important principle must always be kept in mind, and that is never to institute sudden changes in the diet of a patient who has not previously been under treatment, otherwise a comparatively mild case may become severe and acidosis be precipitated. Woodyatt has emphasized this in elderly diabetics who have for a considerable time been suffering from a mild form of diabetes, and even states that it may be better to allow certain of them to excrete traces of sugar, rather than to institute too rigid dietetic measures. In a younger diabetic this would be dangerous advice, which he fully recognizes.

Treatment of the Mild Cases by the So-called Carbohydrate-free Diet.—Many diabetic cases are sufficiently mild to warrant home or dispensary treatment. Many patients are wage-earners and if not too severe, for economic reasons, institutional treatment must be avoided wherever possible. The glycosuria and hyperglycemia may disappear and the tolerance even be increased by a judicious restriction of the carbohydrates. This may be affected by utilization of the following *starch-free diet*, qualitative list, as outlined by Mosenthal.

Starch-free Diet

May Eat.—Soups.—Clear meat broths, which may contain the vegetables indicated below.

Meats.—All kinds of meats, fresh, smoked or cured, except liver; all meats must be prepared without flour or bread-crumbs.

Fish.—All kinds of fish, but no clams, oysters or scallops.

Eggs.—Eggs in any form, prepared without milk, flour or sweetening.

Butter.—Butter, oil and lard.

Cheese.—All kinds of cheese.

Vegetables.—Asparagus, asparagus tips, brussels sprouts, cabbage, cauliflower, celery, cucumbers, egg-plant, endive, greens from beets, kohlrabi, leeks, lettuce, pickles (sour or dill), pumpkin, radishes, rhubarb, sauerkraut, sorrel, spinach, string beans, swiss chard, tomatoes, watercress, wax beans.

Desserts.—Gelatine, jellies (use sour white wine, brandy or coffee for flavoring).

Beverages.—Tea, coffee, and cocoa made from cracked cocoa (cocoa nibs) sweetened with saccharine (without sugar or milk); claret, burgundy, and whisky in moderate amounts; carbonated waters.

Condiments.—Pepper, salt, mustard, oil, vinegar, saccharine.

Must Avoid Eating.—Sugar in any form. Bread, biscuits and cakes in any form. Toast, rice, crackers, oatmeal (and all cereals); sago tapioca, macaroni, vermicelli, potatoes, carrots, parsnips, beets, corn, beans, peas. All fruits fresh, preserved and dried. Jams and jellies. Pastry, puddings and ice cream. Sauces and gravies thickened with flour.

A diet from this list will not be entirely carbohydrate-free, as the green vegetables permitted will yield about 15 gm. of carbohydrate daily. At first, so as not to institute too radical a change it will be wise to permit a carbohydrate intake of from 80 to 100 gm. daily. For this purpose a certain number of Uneeda biscuits may be used where scales are not available. Each Uneeda biscuit contains 5 gm. carbohydrate, 0.5 gm. protein, and 0.5 gm. fat and yields 26.5 calories. The starch of these biscuits has no advantage over other starches and they are mentioned only for their convenience. If one were permitting 80 gm. of carbohydrate daily, then 13 of these could be allowed, yielding 65 gm. of starch, the remaining 15 gm. being made up from the green vegetables. If glycosuria persist after three or four days, then the carbohydrate can be gradually reduced until the patient becomes aglycosuric. By attaining this result for a number of days the patient's tolerance may materially increase so that it may be possible to materially increase the carbohydrate, but always keeping it below the limit at which sugar appears in the urine. In such a rough procedure no consideration is taken of the glucose-yielding power of the proteins or fats.

The Starvation or "Undernutrition" Treatment of Allen and Joslin.—The profession and diabetic patients owe much to F. M. Allen for his demonstration of the beneficial effect of undernutrition and starvation treatment on the diabetes of depancreatized dogs. Later, it was introduced in the treatment of human diabetes, and its chief champion among clinicians has been Joslin. We owe to Joslin, more than to any one else, the spread of a knowledge of how to regulate the diet of diabetic patients. Although Newburgh and Marsh, Woodyatt and others have shown that such low fat intake as this method entails may not be necessary, and although the introduction of insulin has further obviated this necessity, the method has had such a wide vogue that it seems advisable that a general outline of the procedure should be described.

In general terms the method is thus summarized by Joslin:—"*Preparation for Fasting.*—In severe, long-standing, complicated, obese, and elderly cases, as well as in all cases with acidosis, or in any case if desired, without otherwise changing habits or diet, omit fat, after two days decrease protein and halve the carbohydrates daily until the patient is taking 30 gm. or less; then fast. In other cases begin fasting at once.

"*Fasting.*—Fast four days, unless earlier sugar-free, allow water freely, tea, coffee and then clear meat broths as desired.

"*Intermittent Fasting.* If glycosuria persists after four days, give 1 gm. protein, or 0.5 gm. carbohydrate per kilogram body weight for two days and then fast for three days unless earlier sugar-free. If glycosuria remains, repeat and then fast for one or two days as necessary. If there is still sugar, give protein as before for four days, then fast one, and then gradually increase the periods of feeding, one day each time, until fasting one day each week.

"*Carbohydrate Tolerance.* When the twenty-four hour urine is free from sugar give 5 to 10 gm. carbohydrate (150 to 300 gm. of 5 per cent. vegetables) and continue to add 5 to 10 gm. carbohydrate daily (more in mild cases) up to 50 gm. or more until sugar appears, then fast until sugar-free.

"*Protein Tolerance.*—When the urine is again sugar-free decrease the carbohydrate by one-third or more below the carbohydrate tolerance and then add about 20 gm. of protein and thereafter 15 gm. daily in the form of egg-white, fish or lean meat until the patient is receiving from 1 gm. to 1.5 gm. protein per kilogram body weight.

"*Fat Tolerance.*—It is usually desirable, especially in the young, to add no fat until the protein reaches 1 gm. to 1.5 gm. per kilo body weight and the blood-sugar is normal. Then add 5 to 25 gm. daily according to previous acidosis until the patient ceases to lose weight or receives in the total diet 20 to 30 calories per kilogram body weight.

"*Reappearance of Sugar.* The return of sugar demands fasting for twenty-four hours, or until sugar-free. Resume the former diet adding fat gradually and last of all in order to maintain as high a carbohydrate tolerance as possible, sacrificing body weight for this purpose.

"*Weekly Fast Days.* Whenever the tolerance is less than 20 gm. carbohydrate, fasting should be practised one day in seven; when the tolerance is over 20 gm. of carbohydrate cut the diet in half one day each week.

"The foods commonly employed in determining the tolerance for carbohydrate and protein are 5 per cent. vegetables, oranges or grape-fruit, oatmeal or shredded wheat, potato, fish, chicken, lean meat, skimmed milk."

On page 161 is reproduced one of Joslin's diet tables which will be of great service in arranging the diet whether Joslin's low fat and low protein and starvation treatment or any other method of dietetic treatment is used. There are many details in the treatment which cannot be described here. The above outline, however, gives the main steps in his dietetic management. One of the outstanding features is the insistence on undernutrition. Based on his system of dietetic management Joslin has more recently arranged four Tests Diets, one to be taken each succeeding day and containing progressively diminishing amounts of carbohydrate, protein and fat, and a series of twelve maintenance diets each with gradually increasing amounts of these foodstuffs.

Joslin has persistently emphasized the importance of keeping the fat content of the diet low owing to insistence upon the risk of acidosis resulting from a more liberal allowance of fat; as will be noted later many now hold that a higher fat-intake is permissible without the emaciation which this treatment tends to produce and without the risks of acidosis

FOODS ARRANGED APPROXIMATELY ACCORDING TO CONTENT OF CARBOHYDRATES (JOSLIN)

	1%–3%	3%–5%[1]	10%[1]	15%	20%
Vegetables (fresh or canned)	Lettuce Cucumbers Spinach Asparagus Rhubarb Endive Marrow Sorrel Sauerkraut Beet Greens Dandelion Greens Swiss Chard Celery Mushrooms	Tomatoes Brussels Sprouts Watercress Sea Kale Okra Cauliflower Egg Plant Cabbage Radishes Leeks String Beans canned Broccoli Artichokes canned	String Beans Pumpkin Turnip Kohl-Rabi Squash Beets Carrots Onions Green Peas canned	Green Peas Artichokes Parsnips Canned Lima Beans	Potatoes Shell Beans Baked Beans Green Corn Boiled Rice Boiled Macaroni
Fruits	Ripe Olives (20% fat) Grape Fruit		Watermelon Strawberries Lemons Cranberries Peaches Pineapple Blackberries Gooseberries Oranges	Raspberries Currants Apricots Pears Apples Huckleberries Blueberries Cherries	Plums Bananas Prunes

1 gram protein, 4 calories.
1 gram carbohydrate, 4 calories.
1 gram fat, 9 calories.
6.25 gram protein contain 1 gr. nitrogen.

1 kilogram = 2.2 pounds.
30 grams or cubic centimeters = 1 ounce.
A patient "at rest" requires 25 calories per kilogram.

30 grams (1 oz). Contain Approximately.	Carbohydrates G.	Protein G.	Fat G.	Calories.
Oatmeal, dry weight	20	5	2	118
[2] Shredded Wheat	23	3	0	104
[2] Uneeda Biscuits, two	10	1	1	53
Cream, 40%	1	1	12	116
Cream, 20%	1	1	6	62
Milk	1.5	1	1	19
Brazil Nuts	2	5	20	208
Oysters, six	4	6	1	49
Meat (cooked, lean)	0	8	5	77
Chicken (cooked, lean)	0	8	3	59
Bacon	0	5	15	155
Cheese	0	8	11	131
Egg (one)	0	6	6	78
Vegetables 5% group	1	0.5	0	6
Vegetables 10% group	2	0.5	0	10
Potato	6	1	0	28
Bread	18	3	0	84
Butter	0	0	25	225
Oil	0	0	30	270
Fish, cod, haddock (cooked)	0	6	0	24
Broth	0	0.7	0	3

[1] Reckon average carbohydrate in 5% vegetable as 3% —of 10% vegetable as 6%.
[2] Standard foods of constant weight.

he has feared. His method of treatment, however, has been of inestimable value.

It should be recalled that "fasting" or "starvation" days had been long used by Naunyn and others before they had been used in the Joslin procedure. Naunyn emphasized their importance in clearing up traces of sugar in the urine in severe cases and also in helping to combat the acidosis. In Joslin's fasting days the patients are permitted to have tea, coffee, clear bouillon broth, cracked cocoa shells, and plenty of water. These are of no nutritive value and give the patients the impression that they are not actually fasting and so produce a psychological effect.

Emphasis also must be placed on the fact that the green vegetables are thrice boiled. Thus the carbohydrate content of 5 per cent. green vegetables is reduced to 3 per cent. or lower. Useful foods without actual food value are agar agar, skimmed broths, coffee, tea, cocoa shells, cracked cocoa, mineral oil, starch-free bran biscuits and starch-free bran cereal. Agar agar is useful in the form of biscuits as it helps to supply the craving for bread and is bulky. Mineral oil serves as a useful substitute for olive oil in making salad dressing and has no nutritive value.

Treatment with Low Carbohydrate and Low Protein and High Fat Diets.— Marsh, Newburgh and Holly[1] in 1920 and 1922 showed that nitrogen equilibrium could be maintained on a very low protein, low starch diet when enough calories were provided in fat. The same diets but of lower caloric value, were used to render diabetics sugar-free. They claimed that the patient's urine could be rendered sugar-free on this diet when starvation had failed. The large quantity of fat administered in their diet, they claimed, served to diminish the destruction of the body protein as compared with starvation and, therefore, the protein-sparing effect of the fat not only brings about a lower level of sugar metabolism but also lessens the inanition attendant on starvation.

The method as used by these investigators, is briefly described as follows: "When a patient enters the clinic, he is placed on a diet containing from 900 to 1000 calories of which about 90 gm. is fat, 10 gm. is protein, and 14 gm. is carbohydrate. After the patient has been sugar-free for one to two weeks, his diet is increased to about 1400 calories, of which 140 gm. is fat, 28 gm. is protein and from 15 to 20 gm. is carbohydrate. In the case of small individuals this diet is sufficient for prolonged use, and some of them are discharged with instructions to continue it. For larger persons, after another period of trial, a second increase is made reaching 1800 calories, containing 170 gm. of fat, from 30 to 40 gm. of protein and from 25 to 30 gm. carbohydrate. Further additions may be made to suit individual cases.

"In order to prove that our procedure is an improvement over the usual method we must show (1) that glycosuria is avoided in severe diabetes; (2) that this diet does not precipitate acidosis; (3) that nitrogen equilibrium is maintained; and (4) that the patients are able to lead at least a moderately active, comfortable life."

Newburgh and Marsh seem to have shown that their method is successful in effecting all these results. Petrén, of Lund, Sweden, also claims

[1] *Arch. Int. Med.*, 1922, **29**, 97; Newburgh and Marsh: *Arch. Int. Med.*, 1920, **26**, 647.

to use a high fat diet in diabetics with similar success. The method is distinctly revolutionary and is strongly criticized by Joslin who considers the high fat content of the diet to be a menace owing to the risk from acidosis. Many, however, believe that the very low fat diet of the Allen and Joslin treatment is not necessary. Undoubtedly with insulin now available a higher fat ratio is likely to be permitted in the diabetic diets.

Woodyatt[1] has formulated a method of dietetic treatment of diabetes which has many features to commend it. Here also, the fat content of the diet is considerably higher than that permitted in the Allen and Joslin regimen. In speaking of his method he says: "The rationale of the dietetic management in diabetes is to bring the quantity of glucose entering the metabolism from all sources below the quantity that can be utilized without abnormal waste; and to adjust the supply of fatty acids in relationship to the quantity of glucose so that in the mixture of foodstuffs oxidizing in the body, the ratio of the ketogenic fatty acids to glucose shall not exceed limits compatible with freedom from ketonuria. When, as, and if under these conditions of relative rest for the pancreas, the glucose using function improves, then the food supply may be increased gradually in so far as this can be done without disturbing the above relations."

Briefly stated the procedure is as follows: The caloric requirements of the patient are determined by the Du Bois method. The tolerance of the individual for carbohydrates is determined by a trial diet to ascertain the number of grams of glucose he is capable of burning. Recognizing that, in order to prevent acidosis, it is essential that the ketogenic and antiketogenic constituents of the diet should bear a proper relationship to each other and that 1.5 gm. of fatty acids are burnt by 1 gm. of glucose, The amount of fat and protein in the diet are calculated according to the Woodyatt formulæ given on page 157.

It will be seen that there is still considerable difference of opinion existent concerning the best procedure with regard to the dietetic management. All authorites agree that the amount of carbohydrate must be well within the limit of the ability to burn sugar. The difference of opinion concerns chiefly the amounts of protein and particularly of fat that it is safe to allow. With insulin available it is quite possible that the dietetic management will undergo further modifications.

Intarvin in Diabetes.—All the fats of our foods contain an even number of carbon atoms. Many efforts have been made to produce or discover a fat with an uneven number of carbon atoms in the hope that it would be more easily burnt and thus be less likely to produce acidosis. Eventually Kahn succeeded in making intarvin (intarvin margarate) which has an uneven number of carbon atoms. It has been demonstrated that diabetics can take it without the production of acidosis.

Glycerine in Diabetes.—In 1923 McCann and Hannon, and in 1924 H. M. Thomas, Jr., demonstrated the value of glycerine, which has a low carbohydrate equivalent, as an antiketogenic substance in the treatment of diabetes.

[1] Objects and Method of Diet Adjustment in Diabetes, *Arch. Int. Med.*, 1921, **28**, 125.

Insulin.—A brief account of the steps that led up to the discovery of insulin by Banting and his associates has been given in the section on Etiology. The early claims of the discoverer have been amply substantiated. It is the most potent remedy we possess for increasing the ability of the individual to burn sugar and consequently of preventing and relieving the serious complications of the disease. Its discovery has markedly increased the morale of the severe diabetic by creating a much more cheerful outlook on the future. Its use in diabetes complicated by tuberculosis is of inestimable value, in that it enables the tuberculous diabetic to take a more liberal diet and thus increase his resistance to the tuberculous infection.

It must be emphasized, notwithstanding the availability of insulin, that there must be no relaxation of our insistence upon a proper regulation of the diet of all diabetes patients. Proper dieting still remains the basis of therapy whether insulin be used or not.

Insulin is not necessary in the mild cases. These can be readily controlled by regulating the diet. Its use is indicated particularly in the moderately severe and severe types of the disease and in all cases in children. Its administration is imperative in severe cases with large quantities of ketone bodies in the urine. With each succeeding year a larger proportion of all types of diabetes, particularly hospital cases, are being treated with the aid of insulin. There is no valid reason why it should not come into general use by the profession, if the practitioner takes the precaution to familiarize himself with its use and attendant dangers.

Insulin is given subcutaneously, excepting in severe cases of coma in which it may be administered intravenously, accompanied by the oral or intravenous administration of a certain amount of glucose or levulose. In determining the dosage in any individual case it is most important to remember that, with its present potency, 1 unit of insulin is capable of burning 1.5 gm. of glucose. After determining the patients tolerance for carbohydrates, it is easy to calculate the number of units of insulin required daily by dividing the number of grams of sugar excreted in the urine on a given diet by 1.5.

At the present time Eli Lilly and Company are putting insulin (iletin) on the market in four potencies, one having 10 units per cc., another 20 units per cc., a third 40 units per cc., and a fourth with 80 units per cc. They are designated as U 10, U 20, U-40, and U 80 respectively. No doubt potency will be increased with greater experience in the preparation of it. As has been already stated Abel and Geiling have demonstrated sulphur in insulin, and have advanced the view that its potency is dependent upon the amount of "sodium carbonate sulphur" it contains. Later researches may result in its isolation in pure form. For the administration of insulin, one of the two types of Luer "tuberculin" syringes proves very convenient, owing to the fractional divisions of the cubic centimeter scale.

Dosage and Time of Administration.—The number of units used daily must depend upon the indications in each individual case. Five to 10 units once or twice daily may be all that are necessary to render a diabetic,

who excretes a moderate amount of sugar on a previously adjusted diet, aglycosuric. On the other hand, the writer has seen several cases with severe acidosis in which as much as 200 units or more have been required daily. Small doses have a relatively greater effect in burning sugar than do large doses. A dose of 40 units of the U–20 or U–40 strength subcutaneously exerts an effect on sugar utilization for eight hours, according to Woodyatt. The maximum effect is exerted in about four hours. In the majority of cases two doses daily are all that are necessary. They are usually given before breakfast and supper. The carbohydrates should be so divided that the last meal of the day should contain the largest amount, breakfast the next largest amount, and luncheon an amount intermediate between the two. If a patient has been on a fixed diet for some time and it has been decided to use insulin it is advisable to make a moderate increase in the carbohydrate content of the food in order to lessen the risks of a hypoglycemic reaction. For the same reason it is customary to administer the dose of insulin one-half hour before the next meal.

The Hypoglycemic Reaction or "Shock."—The use of insulin is not without its attendant dangers. An overdose may so reduce the blood-sugar that a series of untoward symptoms may occur from the hypoglycemia. Such a reaction is inevitable when the blood-sugar reaches 0.045 per cent. or lower. Premonitory symptoms often appear when the blood-sugar falls even to 0.08 or 0.07 per cent. According to W. R. Campbell, the earliest symptom which most patients describe is a vague, indefinite feeling of uneasiness, an uncomfortable feeling of impending danger. Marked hunger, dilatation of the pupils, tachycardia, pallor, flushing, nervousness and trembling are also early manifestations. As the blood-sugar further falls excitement with emotional disturbances and occasionally vertigo may occur. Profuse sweating, diplopia and incoördination make their appearance. Marked excitement, emotional instability, sensory and motor aphasia, delirium, disorientation, delusions, confusion and bradycardia occur with blood-sugar levels of 0.055 to 0.040 per cent. Campbell states that unconsciousness has not been observed until the blood-sugar has reached 0.035 per cent. Convulsions have been reported in children by Geyelin and others.

Treatment of Hypoglycemia.—With increasing knowledge of the use of insulin hypoglycemic reactions are less frequent. Fortunately, they are easily combated. Every patient should be informed of the premonitory symptoms when insulin is used. Sugar in some form should be administered. This may be given as levulose, which is comparatively easily burnt by the diabetic, in the form of the juice of an orange. Eating one or two lumps of sugar will often clear up the premonitory symptoms. Honey or corn syrup may be used. Only in the very severe reactions are more vigorous measures necessary. In unconscious patients 25 gm. of glucose may be given by intranasal catheter or by rectum. Some have advocated the injection of epinephrine. This is rarely necessary. It probably acts by mobilization of the glycogen of the liver.

Treatment of Complications.—(*a*) *Acidosis and Coma.*—Constant vigilance is necessary to ward off acidosis and threatened coma. The urine should be examined as regularly for the presence of acetone and diacetic

acid as for sugar. Their presence indicates that more fatty acid is being produced than is capable of being burnt by the amount of carbohydrate actually metabolized. Various dietetic procedures have been advocated, as already outlined, to cause the disappearance of these ketone bodies. These need not be outlined in detail again. Joslin has emphasized the view that the ingested fats must be cut to a minimum. Others believe that this marked restriction of exogenous fat tends to increase the amount of fatty acids produced from endogenous fats in consequence of the resulting undernutrition. Woodyatt and others believe that this object is better attained by giving a more liberal allowance of fat but so arranging the foodstuffs that the ketogenic antiketogenic factors should have the proper relationship to each other. Proper adjustment of the diet will in the vast majority of cases cause a disappearance of the acidosis manifestations. With insulin available as the most important means of combating the acidosis, it is only necessary to refer briefly to the other measure that have been heretofore carried out. Naunyn introduced, and many others advocated the use of alkalis to neutralize the effects of the β-oxybutyric acid and thus spare the alkaline reserve of the body. Sodium bicarbonate was the alkali usually administered in large doses by mouth, per rectum, or intravenously in 1 to 3 per cent. solution in normal saline. Joslin believes that alkalis are not necessary and abandoned them with his undernutrition and starvation regimen. However, Campbell with a wide experience with insulin, still advocates the use of alkalis as an aid to treatment.

β-oxybutyric acid is excreted only by the kidneys. Magnus-Levy found that the concentration of these acids in the urine seldom rose above 1.5 per cent. and except in coma he never found values above 0.6 per cent. It is evident, therefore, that the elimination of the acid bodies is closely connected with the quantity of water excreted. It is therefore incumbent to force water if the patient can still take fluids, or to give fluid by rectum, subcutaneously or intravenously as normal saline.

It has usually been customary to increase the carbohydrates in threatened coma cases. Levulose is the easiest burnt of all sugars. It may be given as such or as orange juice. Oatmeal-water gruel is often used and is easily administered. From 50 to 75 gm. of carbohydrate may be given in the twenty-four hours.

Insulin.—In all cases in which the ketone bodies do not disappear by dietetic management; in all cases of severe acidosis as indicated by low blood carbonate and low respiratory quotients, which should be frequently determined; and in all cases of actual coma insulin therapy should be at once instituted. Its administration enables the diabetic to burn more glucose and consequently to burn more fatty acid and thus relieves the symptoms. Even with insulin it is inevitable that lives will still be lost from coma. Patients will enter hospitals or be seen by physicians in private practice in deep coma in which death is so imminent that a fatal termination will occur before the remedy has a chance to act.

The insulin must be given in large amounts in imminent or actual coma. At least 40 to 50 units should be given as an initial dose, half given subcutaneously and half intravenously. Campbell recommends an initial

dose of 100 units, at the same time giving 1 gm. of glucose for each unit of insulin used. This may be given intravenously. After the initial dose from 10 to 20 units of insulin should be given every two to four hours. Small doses frequently repeated are more effective than single large doses. In severe cases a total of from 200 to 250 units in the twenty-four hours may be necessary.

During the intensive treatment of coma with insulin the blood-sugar and CO_2 combining power of the blood should be determined at four-to-six-hour intervals. When the urine becomes free from sugar, the combining power of the blood for CO_2 reaches 40, and the blood-sugar reaches a level of 0.2 per cent. and the patient's general condition has improved, the patient may be placed on the proper dietetic regimen.

In diabetic coma, it is important to move the bowels, preferably by enema, but only after the tissues have retained considerable fluid. Salt should be allowed freely, as it retains fluid in the tissues consequently diluting the concentration of fatty acids and rendering them more easily eliminated by the kidneys. Bicarbonate of soda has also the same effect in causing retention of fluids in the tissues, in addition to favoring the elimination of the fatty acids. Three to 5 gm. in a glass of water every hour or two should be given. In unconscious cases it may be given intravenously in a 3 to 5 per cent. solution. The writer still believes that it is wise to give alkalis. If bicarbonate of soda be used, its administration should be controlled by frequent observations of the blood CO_2 so as to prevent an actual alkalosis. The patient should be at absolute rest, with warm blankets and hot-water bottles about him. For the weak heart action, digitalis hypodermically is indicated.

(*b*) *The Surgical Complications of Diabetes.*—These consist chiefly of gangrene, extensive cellulitis and abscesses, boils and carbuncles. The diabetic in the past has been considered a poor surgical risk for three chief reasons: (1) Owing to the usual advanced age of the patient; (2) owing to the belief that infection is likely to occur, and (3) owing to the frequency with which operations were followed by coma. The tendency, heretofore, has been to avoid or defer operation in diabetics wherever possible. It is well known that the giving of a general anesthetic, ether and particularly chloroform, will raise the blood-sugar of non-diabetics. Their influence on carbohydrate metabolism is even greater in the diabetic. By the use of insulin the risks of coma following operation are reduced to a minimum. Its use is also of the greatest value in quickly getting the patient's blood-sugar to normal. Without it, the previous experience in many cases was that it often took weeks to desugarize the patient with diabetic gangrene. It is a familiar fact that all infections tend to lower the carbohydrate tolerance of diabetics by lowering the endocrine function of the pancreas.

In the pre-insulin days if diabetic gangrene were of the dry type, as it often is, there was a tendency to delay operation until a line of demarcation was established but to operate early if the gangrene were of the moist, rapidly spreading type. It required good judgment to decide when was the most favorable time to operate. It is the writer's opinion that at the present time with insulin available its administration should be started

at once if glycosuria and hyperglycemia are not readily controlled by diet and the surgical procedure got over with. This applies to cases with carbuncle or phlegmon as well as with gangrene. The use of insulin is also of great value in the postoperative treatment, as it will permit of a more liberal diet. Although the fear of infection under strict aseptic precautions should be no greater in the diabetic than in the non-diabetic, it seems safe to say that wound healing is more prompt with the use of insulin. Insulin also is of great value in the surgical care of diabetics who develop acute complications such as appendicitis and empyema.

In amputation for diabetic gangrene the local circulation is always seriously impaired owing to arterial disease. It is, therefore, most important that the circulation of the affected extremity should be carefully studied and that amputation should be performed sufficiently high up to avoid the necessity of the repeated operations that have been only too common in the past.

(*c*) *Pulmonary Tuberculosis.*—The usual hygienic measures are requisite here as under other circumstances. Insulin is proving a most valuable aid in the treatment of the tuberculous diabetic by permitting a much higher caloric diet to be given than was formerly possible.

(*d*) *Pruritus Pudendi.*—In the majority of cases this distressing symptom readily yields when the patients are rendered aglycosuric. In obstinate cases insulin will quickly bring this about. Personal cleanliness and bathing the genitals after each voiding should always be observed. In this way there is less likelihood of hyphomycetal growth in the superficial layer of the skin which tends to keep up the pruritus. In some cases the itching may persist for several days or weeks after the urine has been rendered aglycosuric. Simple ointments such as oxide of zinc, stearate or oleate of zinc may prove soothing in these cases.

(*e*) *Neuritis.*—Neuritic pains prove very intractable in many cases and the patients suffer intensely. The neuritis occurs most frequently in the long-standing, mild cases in middle-aged or elderly patients, who have not or will not adhere to a properly regulated diet. The pains may disappear with the control of the diabetes but too often the neuritic pains persist even after the glycosuria is controlled. Salicylates, pyramidon and other analgesics may be tried. Codeine may be administered with these and will sometimes give temporary relief. Morphia should be shunned, as experience has shown that these cases are only too liable to become morphia habitués.

(*f*) *Pregnancy and Diabetes.*—If a pregnant woman acquires diabetes it is probably best to allow the pregnancy to run its course until contraindicated by inability to control the diabetes. A transient glycosuria in pregnancy may subsequently result in a permanent diabetes. If a diabetic become pregnant, the situation becomes a more serious one, as the pregnant state increases the severity of the diabetes, possibly owing to the disturbed liver function in pregnancy. It is wise to caution diabetic women against the risks associated with the pregnant state. Now that insulin is available the outlook of the pregnant diabetic woman is infinitely more favorable than heretofore.

The Spa Treatment of Diabetes.—There is little to convince one that the particular waters of these various spas have exerted any specific beneficial effect upon the metabolism of diabetics. The fact that Abel and Geiling have found a labile or unstable sulphur compound in their analysis of insulin at least raises the question whether or not those waters of mineral springs containing sulphur may exert a beneficial influence. Undoubtedly the benefits from spa treatments are essentially attributable to the associate dietetic management, which the patients are less inclined to pursue in their own homes. Respite from the nervous strain of business and the living in a pleasant, cheerful environment are additional factors in any improvement resulting.

DIABETES INSIPIDUS

Definition.—A chronic affection, characterized by the passage of large quantities of pale urine of low specific gravity with a low salt and nitrogen content, great thirst, and frequently by evidence of involvement of the pituitary gland or hypothalmic region.

Incidence.—Diabetes insipidus is a rare disease. Up to May 15, 1925, there were only 19 cases in the medical wards of the Johns Hopkins Hospital out of a total of 53,012 patients. From August, 1912 to August, 1925 there were 7 cases in children under twelve years of age under Holand's cases in the Harriet Lane Home among 45,658 admissions. Rowntree, from collected statistics, including 24 from the Mayo Clinic among 257,500 patients, found 127 instances out of a total of 800,000 patients. Among 113,600 patients at the Charité, Berlin, from 1877 to 1896, there were 55 cases, or 0.048 per cent.

Classification.—The cases may be divided into two groups: (1) The primary or idiopathic cases. This group includes the hereditary cases in which it would appear that there must be a constitutional defect, probably in the kidneys or possibly in the pituitary gland. (2) The secondary or symptomatic cases. These include the cases in which there is evidence of organic disease of the pituitary gland or its immediate vicinity.

Although much light has been thrown upon the etiology of the secondary or symptomatic cases, the fundamental cause of the disease in the so-called idiopathic group, particularly when numerous cases occur in successive generations in the same family, still remains to be adequately explained. We can suspect a pituitary disturbance of functional origin but of this there is no convincing proof. On the other hand there may be an inherited inability of the kidneys to secrete a concentrated urine. The classification, as given above, must be considered purely a temporary one and may have to be modified as more knowledge concerning the idiopathic group is acquired.

Etiology.—The majority of cases occur in comparatively *young persons.* Of 85 cases collected by Strauss, 9 were under five years, 12 between five and ten years, 36 between ten and twenty-five years. In van der Heijden's series of 87 collected cases, there were 7 in the first, 19 in the second, 23 in the third, and 19 in the fourth decade. A *hereditary tendency*

has been noted in certain cases. The most remarkable instance of this is in the family reported by A. Weil. Of 91 members of four generations, 23 had persistent polyuria without any deterioration of health, namely, the great-grandfather, his three children, seven grandchildren, and twelve great-grandchildren. Of the 22 affected descendants of the original patient, there were 11 males and 11 females. The cases were congenital and persisted throughout life. Males are more liable to the affection than females. Of our 19 cases, 12 were males and 7 females. Two occurred in colored patients; 1 in each sex.

In 1674 Thomas Willis first differentiated diabetes insipidus from diabetes mellitus by recognizing that the urine of the former possessed an insipid taste. From that date until the last few decades the cause of the disease was the subject of considerable speculation. It gradually became recognized that many of the secondary cases were associated with tumors and particularly fractures of the base of the brain. Various portions of the cerebrum or cerebellum were described, lesions of which were thought to be the potential cause of the diuresis.

In the last twenty-five years, however, increasing evidence has been accumulating to show that a disturbed function of the pituitary gland or its neighborhood is responsible for the symptoms in a large proportion, if not all, of the so-called secondary cases. The first evidence advanced to show that there was a relationship between the function of the pituitary and the urinary output occurred in 1906 when Schäfer and Herring demonstrated that the posterior lobe of the hypophysis cerebri contained a hormone which, when injected intravenously, caused dilatation of the renal vessels and a temporary increase in the flow of urine. This work led to the early misconception that the symptoms of diabetes insipidus were due to an overactivity of the posterior lobe of the hypophysis. In 1912, E. Frank reported a case of diabetes insipidus with typical symptoms in which at autopsy it was found that a bullet had lodged in the sella turcica. From a clinical and pathological standpoint this case was of great significance. In the following year, Simmonds described a case in which the condition was associated with a carcinomatous metastasis in the pituitary complicating a carcinoma of the breast. Additional evidence was advanced by Cushing in 1913. He stated that of his first 100 cases of pituitary disease in 6 the polyuria and thirst had been so marked that a diagnosis of diabetes insipidus had been made before the patients came under his observation. Up to this time, the concensus of opinion was that hyperpituitarism of the posterior lobe was the cause of the disease.

The investigation of Pentimalli and Queriac in 1912 began to throw some doubt on this conception. By perfusion experiments in rabbits they found that the extract of the posterior lobe caused constriction of the renal vessels and diminution of the urinary output. In 1913, Biedl, unable to reconcile the obvious discrepancies, questioned the theory of hyperactivity of the pituitary as the cause of diabetes insipidus, and pointed out its association also with destructive lesions of the gland. In the same year, Farini, in Italy, and von den Velden, in Germany, working independently, experimented with extracts of the posterior lobe and pars intermedia in the treatment of diabetes insipidus and obtained striking

results. Both found a marked restriction of the urinary output. Notwithstanding the fact that von den Velden was the first to actually demonstrate the efficacy of pituitary substance in the treatment of the disease, he failed entirely to appreciate its significance, stating "there is little to favor the idea of substitution therapy." On the other hand, Farini advanced the view that diabetes insipidus was due to a hypoactivity of the posterior lobe of the hypophysis, and deserves the credit for first propounding this now generally accepted view of its etiology.

Since the early observations of Frank and Simmonds the literature contains records of several other cases of diabetes insipidus in which the clinical findings or necropsies showed evidence of pituitary disease. In 1920 Crouzon reported 2 interesting cases in young persons both showing defects in the bones of the skull. One was a young boy with dystrophia adiposogenitalis and exophthalmos. The other was a girl, aged four years, with exophthalmos. Both had diabetes insipidus. The same year Christian reported the case of a child aged five years, with extensive defects of the bones of the skull, exophthalmos, and diabetes insipidus. Cross, in 1922, reported a case of a woman, aged fifty-eight years, with diabetes insipidus and multiple metastases of the bones at the base of the skull. In all these 4 cases it was presumed that there was disturbed pituitary function but no absolute proof.

The view that diabetes insipidus is dependent upon *hypofunction of the posterior lobe of the pituitary* has been opposed by a small group of investigators. Camus and Roussy in 1921 found that puncture of the gray matter in the neighborhood of the tuber cinereum in the hypothalmic region was promptly followed by polyuria in hypophysectomized animals which had not previously shown any signs of diabetes insipidus. Bailey and Bremer obtained the same results. The latter observers also in 1921 found that diabetes insipidus could be produced by puncturing the hypothalmic region in animals whose pituitaries were intact, and in whom sections of the pituitary gland, after the animals were sacrificed, showed that absolutely no damage had been done to the gland by the procedure. Bailey and Bremer found that some of their dogs developed manifestations of dystrophia adiposogenitalis, which led them to think that this syndrome might be dependent on a hypothalmic rather than a pituitary lesion. It is important to observe that Bailey and Bremer found that the injection of pituitrin promptly reduced the polyuria in their experimental dogs. On the basis of their experimental work Camus and Roussy and Bailey and Bremer hold the view that diabetes insipidus is dependent upon a lesion of the hypothalmic region rather than of the pituitary gland.

In the cases of diabetes insipidus following fractures of the base of the skull it is easy to see how a basilar hemorrhage could cause a disturbance of the pituitary or hypothalmus.

In reporting 9 cases of diabetes insipidus the writer found that 4 had *syphilis*, although these were reported before the days of the Wassermann reaction. The subjective symptoms and polyuria in all these cases were helped but not entirely relieved by courses of iodide of potassium. Fournier, Buttersack, Nonne, Oppenheimer, Spanbock and Steinhaus

have emphasized the frequency of the occurrence of polyuria in association with basilar syphilitic meningitis. Several of these have been typical diabetes insipidus cases. It is highly probable that the pituitary was involved in the syphilitic process. Oppenheim considers an "oscillatory" form of hemianopsia or "hemianopsia bitemporalis fugax" as practically pathognomonic of basilar syphilitic meningitis. This ocular manifestation was present in 2 of the 4 patients of diabetes insipidus who had syphilis.

Tuberculous meningitis has been found in several cases. In fact the first case ever reported showing a lesion of the hypophysis associated with diabetes insipidus was recorded by Hagenbach in 1883. The patient had a tuberculous meningitis of the base of the brain with a tuberculous nodule in the infundibulum.

According to Rowntree, the literature reveals 8 cases with actinomycotic abscesses in the neighborhood of the pituitary.

Hadra and Ralfe have reported cases accompanying *aneurism* of the carotid and abdominal aorta. The disease has not infrequently been noted in affections of the abdominal viscera. In 1794, Frank observed a fatal case in a patient with chronic disease of the intestines. Schapiro reported 5 similar cases. Dickinson recorded an instance in a patient with carcinoma of the liver with metastases in the retroperitoneal lymph glands, which had involved branches of the solar plexus.

The disease has been found in association with lesions of the cord, such as tabes, syringomyelia, spastic spinal paralysis, Friedreich's hereditary ataxia. May it not be, in the case of aneurisms, abdominal lesions, and spinal-cord affections, as Cushing and his co-workers believe, that the pituitary function is involved through the influence affecting the nervous tracts passing from the cord to the superior cervical sympathetic ganglion and posterior ganglionic fibres to the pituitary?

Diabetes insipidus has been attributed to exposure, drinking bouts, and ingestion of large quantities of cold fluids. These are very doubtful causal factors. Cases have been reported as developing during convalescence from the acute specific fevers.

In 1905 Eric Meyer advanced the view that in diabetes insipidus we are dealing with a primary polyuria which results from *incapacity of the kidneys to concentrate urine.* In consequence of this supposed incapacity on the part of the kidneys the patient, in order to eliminate the end-products of tissue metabolism, has to imbibe large quantities of water to dilute these end-products down to the limit of the capacity of the kidneys to excrete them. This conception was supported also by Tallqvist and held sway for a few years. Schweenkenbecker, Forschbach and Weber, and Fitz later showed that the concentrating power of the urine in diabetes insipidus is not entirely lost. We also know that the administration of pituitrin restores to the kidney the power to concentrate urine. Other evidence also led to the abandonment of the theory. It was shown that the total renal function and phthalein excretion are normal, and that there was no increase in the blood nitrogen.

Conception that Diabetes Insipidus is Dependent on Hypoactivity of the Posterior Lobe of the Pituitary Gland.—Abundant evidence has

accumulated to show that the disease is dependent in the great majority of the secondary or symptomatic cases upon lesions of the posterior lobe of the pituitary. Rowntree found 21 cases in the literature in which lesions were proved to exist in the pituitary. Of these 3 were tuberculous, 17 neoplastic, and in one a bullet was lodged in the sella turcica. Of the lesions restricted to one portion of the gland he found that in no instance were they limited to the anterior lobe. It is important to emphasize, however, that the literature revealed 6 cases with lesions of the pituitary without associated polyuria. Further convincing evidence of the relation of diabetes insipidus to pituitary disease is the remarkable effect that commercial pituitrin has in reducing the urinary output and thirst.

The researches of Abel, and his associates Geiling and Kolls, with pituitary tartrate, which they have isolated from the pars intermedia and pars nervosa of the posterior lobe, are most illuminating. They believe that this product contains the active hormone of the posterior lobe, although they do not hold as yet that it is in absolutely pure form. Abel says "We have so far failed to find a single activity of a posterior lobe extract referable to a specific principle or principles which is not duplicated by our tartrate and we therefore conclude that the oxytoxic, pressor, respiratory, diuretic-antidiuretic actions of our tartrate are but manifold actions of one and the same active principle or hormone." Injection of this pituitary tartrate in diabetes insipidus yields the same relief obtained from commercial pituitrin. The earlier misconception that diabetes insipidus was dependent upon a hyperactivity of the posterior lobe of the pituitary was in large part due to the fact that injection of pituitrin in animals and normal human beings produced an initial, temporary diuresis. It was later found that the initial diuretic response was followed by a period in which there is a striking antidiuretic effect. The purified pituitary tartrate has this same diuretic-antidiuretic action.

The modern conception, therefore, is that normally water metabolism is regulated by the hormone of the posterior lobe of the pituitary gland through its diuretic-antidiuretic action. If for any reason the ability of the posterior lobe to produce its hormone is impaired or destroyed, such as involvement by tumors, tuberculosis, syphilis or a foreign body, then its antidiuretic function is destroyed and diabetes insipidus ensues with polyuria and attendant thirst.

Abel and Geiling have shown that extracts of the brain substance in the hypothalamic region, both anterior and posterior to the hypophysial stalk, produce, respectively, pressor and pressor-oxytoxic effects. While they have not definitely demonstrated it, they suggest that these extracts may also exert a diuretic-antidiuretic action. They believe that these portions of the brain tissue produce or contain the same hormone as that yielded by the pars intermedia and pars nervosa of the posterior lobe. If this be the case, they think that it affords an explanation for the failure of diabetes insipidus to occur in hypophysectomized animals until puncture of the hypothalamus has been performed. They throw out the suggestion that in the hypophysectomized animals sufficient hormone producing tissue remains intact in the hypothalamus to prevent the symptoms of diabetes insipidus from developing, in the same way that the islands

of Langerhans present in the remaining one-tenth of the pancreas will prevent diabetes mellitus from developing in animals after nine-tenths of the pancreas has been removed. They also suggest that the symptoms of diabetes insipidus produced in animals by Bailey and Bremer by puncturing the hypothalmus with the pituitary intact may be explained either by an interference with the production of the hormone of the pars intermedia and pars nervosa, or by interference with its transference to the cerebrospinal fluid or to the blood stream or both.

All the etiological problems of diabetes insipidus are not yet solved. Subsequent investigation may show that the so-called primary or idiopathic cases are really dependent upon pituitary diseases in an early stage. Pituitary tumors may exist for many years without producing neighborhood symptoms that lead to their recognition. The hereditary cases are hard to explain. Should it be demonstrated that they yield to pituitary therapy, this will be strong evidence that even they are due to a deficiency of the production of the hormone of the posterior lobe.

Morbid Anatomy.—There are no lesions peculiar to the disease. The various morbid processes found at autopsy are primary rather than secondary. The kidneys are usually enlarged and hyperemic. The bladder is dilated, and its walls hypertrophied. Dilatation of the ureter and pelves of the kidneys is occasionally found.

Symptoms.—The disease may begin abruptly but more commonly it develops slowly. *Polyuria* is the most constant and characteristic feature. The daily quantity of urine may be enormous. Trousseau had a patient, aged twenty-four years, who passed 43 liters in a day. The weight of the urine voided daily may almost equal that of the patient; Vierordt cited an instance of a child weighing 13.2 kilograms, voiding 12.3 kilograms of urine daily. The largest daily elimination in any of the writer's 9 cases was 16.5 liters. One passed 1700 cc. at a single voiding. The urine is usually almost colorless, but may have a bluish tint. The specific gravity generally ranges between 1.001 and 1.005. Albumin may be present. Rowntree found that 16 of his 24 patients showed traces of albumin at some periods of their study. The output of urine may exceed the intake of fluids. The balance of opinion favors the view that a condition of "bradyuria" rather than "tachyuria" exists in this disease. In other words, when a copious draft of fluid is taken, an increase in the flow of urine is slower in making its appearance, and the total elimination is slower in a patient with diabetes insipidus than in a healthy individual. Muscle-sugar, or inosite, has been frequently demonstrated in the urine. This is believed to result from the flushing out of the muscles by the enormous quantity of fluids.

In rare instances a mild diabetes mellitus may pass over into a diabetes insipidus. This is most likely to occur in traumatism of the brain, in which at first glycosuria accompanies the polyuria, but later disappears, leaving the characteristic urinary features of diabetes insipidus. Occasionally, however, diabetes insipidus may pass over into diabetes mellitus.

The total renal function and phthalein excretion are normal, and there is no increase in the blood nitrogen.

Thirst is practically a constant and often a distressing symptom. In many cases it is the first one complained of, as it first attracts attention. One patient of the writer said he "simply lived to drink," and described the infinite satisfaction it gave him to be able to take a whole pitcher of water at one draught. Trousseau's patient drank 50 liters in twenty-four hours. In experiments in which the fluids have been cut off, the patient has been known to drink his own urine. In a traumatic case in the Johns Hopkins Hospital a boy, aged fifteen years, had frequent convulsions. He drank enormous quantities of water and the convulsions recalled those produced in dogs by Rowntree following administration of large quantities of water by a stomach tube.

The appetite varies considerably; often it is not increased, and may be diminished or it may be ravenous, as in Trousseau's patient, who ate in the Paris restaurants, where the meals were at a fixed price and the bread was not charged for. He devoured so much of the latter that it was more profitable for the restaurant keepers to pay him to remain away. In these bulimia cases there is a marked increase in the urea output. Absence of sweating is the rule; the insensible perspiration is also diminished. Constipation is common. Cataract has been described. One of the writer's patients has bilateral plaques of xanthoma palpebrarum. There may be recurring attacks of transitory bitemporal hemianopsia in cases due to basilar syphilitic meningitis. Choked disk may be present. Paralysis of the sixth nerve is sometimes seen. Many of the cases due to cerebral disease have intense headaches. Some suffer early and throughout the disease, with racking pains in the back and legs. In one of the writer's cases there were several attacks of transitory left-sided hemiplegia, followed by an attack of longer duration, from which it took weeks to recover. Impotence not infrequently occurs. Marked emaciation may develop in the secondary symptomatic cases. In the idiopathic cases, on the other hand, there may be no loss in weight. Œdema of the feet may occur in the last stages of the asthenic cases. The knee-jerks are likely to be exaggerated; in 9 cases, they were exaggerated in 5, normal in 1, diminished in 2, and not noted in 1. The metabolism is but little disturbed, notwithstanding the abnormal fluid exchange. In some cases the blood is concentrated and the red cells may be between 6,000,000 and 7,000,000 per cmm. The temperature is always subnormal, unless some complication intervenes. During febrile attacks the amount of urine may diminish considerably. The pulse is usually of small volume, and there is said to be no increase in the blood-pressure. Toward the end the exhaustion may be extreme. Death is sometimes preceded by an uncontrollable diarrhœa. Drowsiness eventually ensues, and death occurs with the patient in coma. The immediate cause in many cases is a low form of congestive pneumonia.

Diagnosis.—There is no arbitrary line separating the physiological from the pathological polyurias, so far as the amount of urine is concerned. The chief distinguishing feature of the polyuria of diabetes insipidus is its permanence, a physiological polyuria usually being transitory. The greatest difficulty arises in distinguishing the cases from those of chronic interstitial nephritis. In the latter, the existence of albumin

and a few casts, with certain cardiovascular features, should prevent much difficulty. The hysterical polyuria is usually recognized by the existence of certain nervous and psychical symptoms and the polyuria is likely to be intermittent in character. Some have included hysterical polyuria as a form of diabetes insipidus, but this hardly seems justifiable. The absence of sugar and the low specific gravity differentiate the affection from diabetes mellitus.

Special attention should be paid to the discovery of some cerebral lesion, particularly of pituitary origin. Careful search for the ocular and other neighborhood symptoms of pituitary tumor should be made. In the presence of demonstrable pituitary disease, the diabetes insipidus may be considered an evidence of hypofunction of the posterior lobe of the pituitary.

The most important procedure in the differential diagnosis is the application of the therapeutic test, the polyuria disappearing on the subcutaneous injection of the extract of the posterior lobe and pars intermedia. Whether a negative result indicates absence of a true diabetes insipidus must be determined by subsequent experience. It has not been definitely determined whether both primary and secondary types respond equally well to pituitary extract. Some cases have been reported as responding to treatment in which no demonstrable signs of cerebral or pituitary disease have been present.

Prognosis.—Idiopathic diabetes insipidus is much the more benign of the two forms. There is usually no marked emaciation, and the duration has been fifty years. The prognosis is less favorable in the secondary or symptomatic cases. Emaciation is often rapid and an early fatal termination may ensue. The length of life depends largely on the seat and nature of the causal organic lesion.

Treatment.—Since the demonstration that extracts of the posterior lobe of the pituitary caused a marked reduction in the urinary output and thirst in diabetes insipidus cases, this treatment, a substitution therapy, has come into general use and has given excellent results in most cases. As a rule surgical pituitrin (which is double the strength of obstetrical pituitrin) is used. In many cases 1 cc. of surgical pituitrin once daily will control the polyuria and thirst. Rowntree states that in in one of his patients the polyuria was controlled for four days by one injection. In very severe cases, not controlled by 1 cc. daily, two injections of 1 cc. in the twenty-four hours may be tried. These larger doses may cause intestinal cramps, and to obviate this Barker and Mosenthal suggest smaller doses at more frequent intervals. An output of from 10 to 12 liters daily often falls to 2 to 3 liters. It has usually been found that the effect of a single dose of 0.5 to 1 cc. of the extract lasts only seven to eight hours.

Patients, naturally, object to hypodermic injections, so it is satisfactory to find that Blumgart demonstrated that the symptoms were relieved as well by intranasal spraying as by subcutaneous or intramuscular injection. Larger doses, are said to be required. Five cubic centimeters was the maximum amount used at one time as a spray. McCann obtained excellent results with this method when subcutaneous injections failed.

The patient was given a spray containing 1 cc. of surgical pituitrin in normal saline solution and used it frequently during the twenty-four hours. Oral administration has proved ineffective.

The numerous drugs employed, chiefly ergot, opium and valerian, have very little effect; when syphilis is present, vigorous treatment with iodides, mercury and the newer arsenical preparations should be pushed. When there is evidence of actinomycosis of the base of the brain iodide of potassium should be administered.

Surgical procedures are indicated when there are definite evidences of pituitary tumor. Removal of the tumor may permanently cure the polyuria and thirst, and obviate the necessity of continuing the pituitary extract, which otherwise has to be kept up, as it is merely substitution therapy. The extract may have to be continued if the posterior lobe is entirely destroyed or removed.

Meyer claimed to have obtained improvement by giving theocin on the belief that it increased the ability of the kidney to concentrate urine. The dosage is 0.2 gm. (3 gr.) three times daily. It has been shown to have very little effect.

Dietary control is of subsidiary importance. The amount of fluid intake may be gradually reduced so long as there is a reduction in the urinary output. The thirst is best met by giving acidulated drinks. Tallqvist recommends a gradual reduction of salt and protein in the diet.

If specific therapy with pituitary extract fails to give results, the various older procedures should be given a thorough trial.

CHAPTER III

GOUT

By THOMAS B. FUTCHER, M.B.

Definition.—A disorder of purin metabolism characterized by an excess of uric acid in the circulating blood and diminished excretion of uric acid in the urine, and, usually, by an arthritis, the distinguishing feature of which is the deposition of sodium urate in the peri-articular cartilages and tissues. It derives its name from *Gutta*, which came into use in the XIIIth Century and signifying the drop of evil humor distilled into the joints.

Incidence.—Gout is more common in England than elsewhere in the world. Llewellyn, an English authority, writing in 1921, stated that the incidence had diminished in the previous twenty years; Allbutt was of the same opinion. Although less common in the United States, the cases, if tophi in the ears are searched for, are more frequent than is generally supposed. In the medical wards of the Johns Hopkins Hospital there were from 1889 to May 15, 1925, 124 cases among 53,012 medical patients or 0.23 per cent. of the cases. The writer found that a comparison of the number of cases admitted to the Johns Hopkins Hospital with those admitted to St. Bartholomew's Hospital during a period of fourteen years showed the ratio of gout admissions to be 2 to 3. Pratt reports that only 61 cases were treated in the wards of the Massachusetts General Hospital from 1821 to 1923. On the other hand Williamson, in 1920, states that 116 cases were admitted to the Cook County Hospital, Chicago, during a period of six years. Tophi were present in the ears in 65. The percentage of gout to the total admissions was 0.39, whereas, in statistics of St. Bartholomew Hospital, it was 0.37. This would seem to show that gout is even more common in Chicago than in London, among the hospital population. Pratt, who has been the most active student of the disease in this country, while of the opinion that gout is comparatively rare in the United States, has shown clearly that, when the attention of clinicians is directed toward the manifestations of the disease, more cases become recognized. He found that from the opening of the Massachusetts General Hospital in 1821 until 1910 there were only 29 cases in the wards diagnosed as gout, whereas 32 cases were recognized from 1910 to 1923.

Etiology. 1. **Predisposing Causes.**—(*a*) *Heredity.*—Hereditary predisposition is, undoubtedly, one of the most important factors and plays a part in from 50 to 75 per cent. of the cases. This is particularly true with the well-to-do class. Scudamore states that out of 523 gouty patients, 309, or 59 per cent., gave a history of the disease in the parents or grandparents. Garrod found that the predisposition was inherited in 50 per cent. of his hospital patients. In his private cases, however,

he believed that the tendency was inherited in 75 per cent. In the first 63 Johns Hopkins Hospital cases there was a history of gout or "rheumatism" in 20, or 31 per cent. It would appear, therefore, that gout in the United States is acquired or "free-hold," rather than inherited or "copy-hold," to use the classification of Sir William Browne. It is an interesting feature that, although the women of gouty families may escape gouty manifestations, they are more likely to transmit the disease to their offspring than are the men. A grandson may inherit gout from a gouty grandfather through a mother who has never shown any manifest symptoms of the disease. Gout acquired from extrinsic causes may be transmitted to the offspring.

(*b*) *Age, Sex, and Race.*—Although, in inherited gout, infants at the breast have shown manifestations of the disease, it is a rare affection in infancy and childhood. This is illustrated by Scudamore's statistics of 515 cases, in which only 4 occurred before the age of seventeen, the youngest being eight years old. There were but 13 in the first two decades. When gout appears in a very young person it is nearly always inherited. In our series of 124 cases, the ages on admission to the hospital, according to decades were as follows: One to ten, none; eleven to twenty, 1; twenty-one to thirty, 5; thirty-one to forty, 21; forty-one to fifty, 42; fifty-one to sixty, 34; sixty-one to seventy, 17; seventy-one to eighty, 4; The general statement is that the initial attack makes its appearance most frequently in the fourth decade.

Males are much more liable to the disease than females. In fact it is rare in women until after the child-bearing period is over. Since the time of Hippocrates, the relative immunity in women has been attributed to the influence of the catamenia. Of 80 cases collected by a special commission of the French Academy, only 2 were in females. Of 124 cases admitted to St. Bartholomew's Hospital, in fourteen years, 24 were in women. In our series of 124 cases, there were only 7 females. Gout in women is usually inherited. Their relative immunity is undoubtedly due, in large part, to their not being exposed to the exciting factors to the same extent as men are.

The colored race does not escape. In the Johns Hopkins Hospital series there were 6 male negroes.

(*c*) *Alcohol.*—It is probable that alcohol heads the list in importance among the predisposing causes. The fermented beverages, particularly port and sherry, beer, ale, and porter, are much more injurious than the distilled liquors. The quality of the alcohol seems to be as important as the quantity. In Scotland, where whisky is the prevailing drink, gout is much less prevalent than in southern England, where beer and heavy ales are the chief beverages. Investigation has failed to explain this difference in the action of the alcohol. It is apparently not due to the greater acidity of the fermented beverages, nor to the greater percentage of sugar or salines contained in them. The analysis of our series seems to show that beer is the chief etiological factor in the United States.

(*d*) *Food and Exercise.*—Gout undoubtedly is a penalty of high living. Rich, nitrogenous foods, particularly the red meats and game, have always been held to be especially injurious. There is a growing tendency,

however, to place less importance on the quality of the food and more on the quantity, and habits in regard to exercise. Overeating and the leading of a sedentary life are probably most important factors. Sydenham stated the case clearly when he wrote: "Great eaters are liable to gout, and of these the costive more especially. Eating as they used to eat, when in full exercise, their digestion is naturally impaired. Even in these cases, simple gluttony and free use of food, although common incentives, by no means so frequently pave the way for gout as reckless and inordinate drinking." Neither the quality of the food nor its quantity does so much harm as the fact that it is "unearned by muscular exertion," as Ewart puts it. We must remember that gout is not confined to the rich, however. Osler says: "In England the combination of poor food, defective hygiene, and the consumption of excessive malt liquors, makes 'the poor man's gout' a common affection." These were the conditions that largely prevailed in our series.

(*e*) *Effect of Lead.*—Musgrave, Huxham, and Falconer (1772) called attention to the association between lead-poisoning and gout, but it remained for Garrod to show the importance of lead as an etiological factor. He found that 33 per cent. of the gout patients that came under his care in hospital practice, had at some period of their lives suffered from lead-poisoning, and had for the most part been plumbers or painters. An analysis of our first 63 cases showed only 3 with positive evidences of lead poisoning. Six others had occupations exposing them to possible lead poisoning. Of the 9 patients, 6 were painters, and 3 were tinners. Thus in 9 of the 63 cases, or 15 per cent., lead was probably a contributory etiological factor.

We do not know in just what way lead poisoning predisposes to gout. Garrod found that the blood of patients suffering from lead-poisoning contained an excess of uric acid. He pointed out also that these patients were liable to develop chronic nephritis, and drew the conclusion that the increased amount of uric acid in the circulating blood resulted from a renal insufficiency. The majority of subsequent investigators have supported this view. Sir Dyce Duckworth held that the lead acts injuriously through its effects produced on the nervous centres.

(*f*) *Occupation and Physique.*—Those whose occupations bring them into constant contact with lead, such as painters, plumbers, and enamellers and to a less extent, tinners, are liable to be attacked. Bartenders and employees in breweries, owing to the opportunity for free indulgence in malt liquors, are also very prone to the disease. One rarely sees gout in a weakly, undersized, and poorly-nourished individual. Persons of large frame, good physique, and with a tendency to obesity, are the ones who usually manifest the disease.

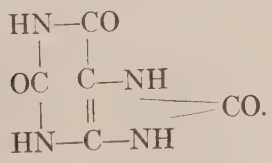
(*g*) *Traumatism* is thought by many to be a contributory factor. The prevalence of the attacks in the big toe-joints has been in part explained by the liability of this articulation to injury while walking or from pressure by an ill-fitting shoe.

2. **Metabolic Causes.**– With the exception of diabetes mellitus and nephritis, no other disease has been the subject of more intensive study from the standpoint of the laboratory investigator. Notwithstanding

the enormous amount of work that has been done, we have to admit that, even to-day, there is still lacking a perfectly satisfactory explanation of the etiology of gout from the standpoint of the chemical changes that are at the foundation of the disease. It is generally conceded, however, that the symptoms of gout are dependent upon a disturbance of the intermediary metabolism of the purin bodies, of which uric acid is the outstanding member. Since uric acid was first isolated from the urine by Scheele in 1776, and since Wollaston in 1797 demonstrated that tophi contained uric acid, the prevailing opinion of students of the disease has been that gout is dependent in some way upon the formation or deposition in the tissues, or elimination of this acid. Upon one point all investigators of the disease are agreed, and that is that in gout there is an excess of uric acid in the circulating blood. This fact, and the fact that the tophi about the joints and elsewhere are composed of the salts of uric acid, have been the chief basis for the generally accepted view that the symptoms of gout are dependent upon the action of uric acid. It has not yet been definitely settled whether the deposition of uric acid in cartilage and fibrous tissue is dependent upon the excess of uric acid in the blood alone, favored possibly by the fact that these tissues are less vascularized and richer in sodium chloride, or whether some primary change must first take place in these structures which later results in the deposition of the uric acid salts.

(*a*) *Uric Acid Metabolism under Normal Conditions.*—To better appreciate the metabolic disturbances in gout, it is important to understand, as fully as our present knowledge permits, the chemistry of uric acid and its closely allied compounds under physiological conditions.

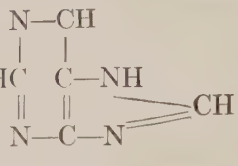
Uric acid has the empirical formula $C_5H_4N_4O_3$ and the rational formula,



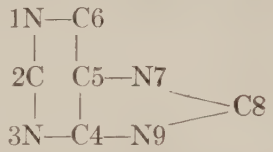
The generally accepted view, at the present time, is that it is derived partly from nuclein resulting from the disintegration of cell nuclei, and partly from the hypoxanthin, which is produced as a product of muscle metabolism. At least 4 other nitrogenous compounds are known to be derived from nuclein. These are xanthin ($C_5H_4N_4O_2$), hypoxanthin ($C_5H_4N_4O$), guanin ($C_5H_5N_5O$), and adenin ($C_5H_5N_5$). In addition to these, there are 5 other compounds closely allied to them in general structure. They are as follows: Heteroxanthin ($C_6H_6N_4O_2$), paraxanthin ($C_7H_8N_4O_2$), episarkin ($C_4H_6N_3O$), carnin ($C_7H_8N_4O_3$), and epiguanin ($C_6H_7N_5O$).

These 10 nitrogenous compounds were named alloxuric bodies by Kossel and Krüger, whereas the last 9 constitute the alloxuric, xanthin, or nuclein bases. The term "alloxuric" was applied because each was made up of a combination of an alloxan and urea nucleus. Emil Fischer has shown that there is a very intimate relationship between the various members and demonstrated that a number of them can be prepared

synthetically. He found that they are all derived from a compound $C_5H_4N_4$, which he termed "purin," having a carbon-nitrogen nucleus, the "purin nucleus," as a basis. Purin, according to Fischer, has the formula

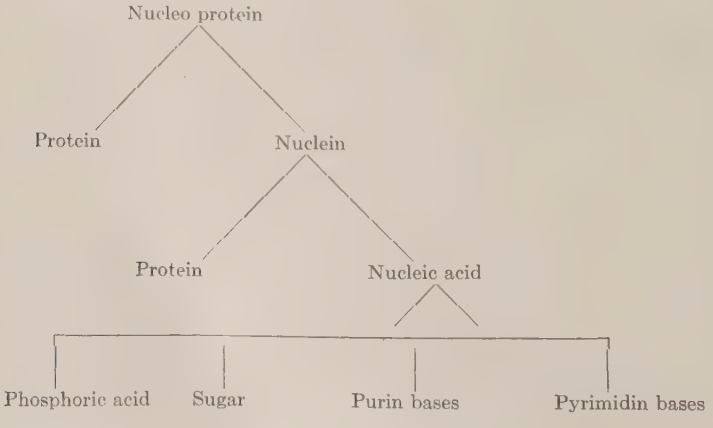


and the different purin bodies are derived therefrom by the substitution of the various hydrogen atoms by hydroxyl, amine, or methyl groups. In order to designate the different positions of substitution, Fischer proposed to number the 9 atoms of the purin nucleus in the following way:



In studying the structural formula of uric acid given above, it will therefore be seen that it is 2.6.8 trioxypurin. Xanthin, accordingly, is 2.6 dioxypurin; hypoxanthin is 6. oxypurin; adenin is 6. amino purin; and guanin is 2. amino 6. oxypurin, etc. To summarize, therefore, the alloxuric or purin bodies include uric acid, together with the alloxuric, purin, nuclein, or xanthin bases. The purin substances are supposed to be contained in the nucleic acid of the cell nuclei in the form of a loosely combined phosphorus-containing body—the nucleotin-phosphoric acid, as Schmiedeberg has termed it. Intimately related to the above purin bases are the vegetable bases, caffeine, theobromine, and theophyllin, all of which are methyl xanthins.

That the purin bases, are disintegration products of nucleic acid which is found in the nuclei of all animal and plant cells was the epoch-making discovery of Kossel. Nucleic acid is found in cells in combination with various proteins, called nucleoprotein. Pratt illustrates the disintegration of nucleoproteins by the following diagram:



The purin bodies, from which uric acid is mainly if not entirely derived, come from two sources. Burian and Schur have designated them the "exogenous" and "endogenous" purins. The exogenous purins are those introduced with the ingested food, whereas the endogenous purins are those derived from the nucleins of the body and, apparently, chiefly from muscle metabolism. In the same manner, we speak of "exogenous" and "endogenous" uric acid, when it is derived from these respective sources. By the use of a purin-free diet (such as milk, eggs, butter, cheese, white bread, rice, sago, and fruits) it is possible to estimate the quantity of nuclein derivatives or purin bodies which arise solely as a result of cellular processes. In 1905 Burian demonstrated that the muscle purins, particularly hypoxanthin, are the chief source of the endogenous uric acid. He found that muscular exertion is always accompanied by a decided rise in the output of uric acid. Burian and Schur showed that the endogenous purins excreted in the urine in twenty-four hours vary from 0.1 to 0.2 gm., expressed in terms of nitrogen, of which one-fiftieth to one-tenth is in the form of xanthin or purin bases and the rest as uric acid. On such a diet, Rockwood, working in Chittenden's laboratory, found that the daily output of uric acid in a normal individual ranges between 0.3 and 0.4 gm. He confirmed the observations of Burian and Schur, that a given individual shows a certain degree of constancy in the daily excretion of uric acid. In other words, the elimination of endogenous uric acid is constant for each individual; that is, it is an individual factor dependent, probably in part, upon the weight of the individual or of the contained organs and tissues.

Our knowledge of the successive stages through which the nucleins pass to the end-products of their metabolism has been worked out in detail. The studies of Walter Jones, Schittenhelm, Brugsch, Burian, Levene and others have shown that there is a successive series of specific enzymes concerned in the breakdown of the nucleic acid derived from nuclein. Each enzyme is adjusted to ensure the occurrence of each particular step in the process. This information has been acquired by investigations on animals and the human individual and by ascertaining in what glands the respective enzymes are operative.

Nucleic acid, derived from nuclein, occurs in the form of simple nucleic acid called a mononucleotid and a complex nucleic acid composed of four mononucleotids and called a tetranucleotid. A simple nucleic acid is made up of a molecule of purin or a molecule of pyrimidin united to a molecule of phosphoric acid.

The various enzymes operate in successive steps. (1) *Nucleinase* transforms nucleic acid (tetranucleotids) into mononucleotids. (2) *Nucleotidase* splits the mononucleotides into phosphoric acid and nucleoside. (3) *Nucleotidase* converts the nucleoside into sugar and the purin bases and pyrimidin bases. (4) *Desamidase* has the power of splitting off the amino group NH_2 from the purin bases. The enzyme which thus converts adenin into hypoxanthin is called *adenase*, and that which transforms guanin into xanthin is termed *guanase*. (5) The *oxidases* oxidize xanthin and hypoxanthin into uric acid and are found only in the liver of man. (6) The uricolytic enzyme, *uricase*, the ferment which converts

uric acid into allantoin, is found in all the lower animals, but is absent in man and the higher apes. In lower animals the final product of purin metabolism is believed to be allantoin, practically no uric acid being found in the urine, whereas in man the end-product is believed to be uric acid, although definite proof of this fact has not yet been determined.

Jones and his pupils have found that dog's liver contains *guanase* that deaminizes guanin to xanthin, but not *adenase* which converts adenin to hypoxanthin. In human beings, *adenase* is not present in any of the organs; *guanase* is present in the kidneys, liver and lungs, but not in the spleen or pancreas. The belief exists that guanin can be deaminized to xanthin in any of the organs in which the ferment is found, but not in others, and that adenin is not changed in the human being at all. *Xanthin oxidase*, which oxidizes xanthin and hypoxanthin into uric acid, is found in human beings in only one organ, namely, the liver. It seems probable, therefore, that the liver is the site of the formation of uric acid in human beings.

It is generally conceded that the fate of the exogenous purins, that is those taken in the food, is the same as that of the endogenous purins. They are subject to the same changes noted above as a result of the action of the various enzymes. Recognizing the fact that, on a purin-free diet, the output of uric acid is constant for each individual, it is readily understood that, in the normal individual, the amount of uric acid excreted in the urine is largely dependent upon the amount of exogenous purins taken in the food. It must be remembered that the animal body can synthesize the purin bases of its tissue purins from the amino-acids of protein. To what extent this occurs is not definitely known.

The exogenous purins of the food are contained chiefly in the glandular tissues, such as liver, kidneys, thymus (sweet-breads), brain, and skeletal muscles. Tea, coffee, and cocoa contain the methyl purins theophylline, caffeine, and theobromine and may yield small amounts of uric acid, although this has not been convincingly demonstrated.

Much of our information concerning the quantitative amounts of uric acid in the urine, blood and tissues was unreliable owing to our not possessing a satisfactory and accurate method of determining the uric acid. Since the introduction of Folin's colorimetric method, which has come into general use, this objection has been removed.

Normally, the blood contains from 1 to 3 mg. of uric acid per 100 cc. McClure and Pratt put the upper limits at 3 mg. per 100 cc. This is on a purin-free diet. In the normal individual on a mixed diet the amount of uric acid excreted in the urine ranges between 0.4 and 1.0 gm. in the twenty-four hours. Hammarsten gives the average as 0.7 gm. Fine found that in normal individuals the tissues contain an amount of uric acid comparable to that in the circulating blood.

According to a publication of Gudzent in 1924, the urine is not the only body secretion in which uric acid is eliminated. He found that certain amounts are eliminated in the sputum, tears, nasal secretion, bile, and intestinal secretions, to be in part destroyed by bacterial action and in part to be reabsorbed again. He found that the saliva contained uric acid in about the same concentration as that of the blood. In the bile the

percentage was sometimes even higher than in the blood. Gudzent offers the suggestion that these channels of excretion may account for the variations in the published amounts of uric acid in health and disease.

Much work has been done on the effect of the administration of various purins by mouth or intravenously on the output of uric acid. Krüger and Schmid, in 1901, showed that each of the purin bases, guanin and adenin, when administered to man gave an increase in the output of uric acid. They also found that when hypoxanthin and adenin were fed to human beings, 62 per cent. and 40 per cent. respectively were eliminated in the urine as uric acid.

In 1924, Folin, Berglund and Derick published the results of an investigation on the fate of uric acid when injected into the circulation of various animals and of human beings. In dogs, cats, rabbits and goats as much as 0.2 per cent. of the uric acid is stored in the kidneys, which become œdematous and enlarged. The excretory function of the kidney may be temporarily diminished up to pure inhibition. They found that all other tissues seemed to be impermeable to soluble urates. They also found that the uric acid which was not deposited in the tissues and remained in the blood was rapidly destroyed. Not less than 70 per cent. is destroyed in ten minutes. They state that "the uric acid destruction stops the instant the blood is removed from the living animal. Some unknown essential factor, therefore, must be contributed by the tissues, or by some tissue—possibly the liver. The unknown oxidizing agency is used up as rapidly as it is poured into the blood. This agency, therefore, can scarcely be an enzyme."

These observers found that intravenous injections of uric acid (20 mg. per kilo in the form of lithium urate) into normal men are followed by excretions of from 30 to 90 per cent. The destruction in man, therefore, amounted to from 10 to 70 per cent., the average being about 50 per cent. The duration of the excretion period in man was from one to four days, the duration being determined by the speed of destruction.

They state that the unique and characteristic high levels of uric acid in normal human blood are due to a lack of responsiveness on the part of the human kidney to excrete uric acid. This is apropos of the fact that human blood contains much more uric acid than does the blood of any known animal. This lack of sensitiveness, they assert, is probably a feature of the uric acid absorbing power, rather than of the power to excrete any uric acid that has been absorbed. They found that high protein diets increase the responsiveness of the kidneys and thus lower the level of circulating uric acid. Because of these lower levels less uric acid is destroyed and this is the reason why more endogenous uric acid is excreted on high protein than on low protein diets.

Form in which Uric Acid Circulates in the Blood.—Although this question remains to be definitely settled, most biochemists are in agreement with Gudzent, who believes that it circulates as urate of soda, or, in other words, as the monosodium urate, in which one of the hydrogen atoms of the uric acid is replaced by an atom of sodium. Gudzent believes that there are two isomeric forms of uric acid, differing in the position in which the hydrogen atoms are linked to the molecule. He

calls the two forms "lactam" and "lactim" uric acid. These differ in their solubility in water. Gudzent found that when sodium urate was agitated with water the amount taken up increased up to a certain time, when saturation occurred. By continuing the agitation for a longer time less of the salt was found in solution. Gudzent's explanation for this is that the salt goes into solution first as the salt of the lactam acid, but that in time a tautomeric change takes place in the compound, whereby it is changed to the lactim type, which is only 70 per cent. as soluble as the former. He found also that the lactam salt is more soluble than the lactim salt in blood serum, 18.4 mg. of the former and only 8 mg. of the latter dissolving in 100 cc. of blood serum.

Schade, Boden, Bechhold and Ziegler claim that the monosodium urate of the blood exists in colloid form. Gudzent, Kobler and Lichtwitz deny this. The prevailing opinion is that it occurs in crystalline form. The monosodium urate is contained in the red cells as well as in the serum.

There is evidence that the amount of uric acid in the blood as estimated by the Folin and Wu method does not record all the uric acid. Some of it appears to exist as "bound" or "combined" uric acid. In 1915, Benedict working with ox blood, found in one specimen 0.56 mg. uric acid. After boiling an equal quantity of the same blood with HCl it yielded 5.87 mg. uric acid. Bernstein and Griesbach have found that 50 per cent. of the uric acid of human blood exists as "bound" uric acid.

(*b*) *Uric Acid Metabolism in Gout.*—There is definite evidence indicating that purin metabolism is markedly disturbed in gout. Clinically, this is manifested by the deposition of the urates, often in enormous quantities, in and about the joints, in the bursal sacs and in the cartilages of the ears. We find alterations in the quantity of uric acid contained in the blood and that excreted in the urine, as compared with the normal individual. We find that the gouty patient responds differently from the healthy person, so far as the uric acid content of the blood and urine is concerned, when they are fed rich purin foods. Some of the earlier views concerning the metabolism in gout were incorrect, owing to the fact that the workers did not at the time possess an accurate method of determining the uric acid quantitatively in the blood and urine. The Folin and Wu method, described in 1919, gives us an accurate and reliable method of determining the "free" uric acid in blood and urine. What part the "bound" uric acid of the blood plays in the disturbed metabolism of gout remains to be demonstrated; as yet we are not taking this into account nor has there apparently been devised a satisfactory method for its quantitative determination. Benedict's discovery that boiling ox blood with HCl liberates the "bound" uric acid is an important observation.

Uric Acid in the Blood in Gout.—Normally the blood contains from 1 to 3 mg. of uric acid per 100 cc. The generally accepted view is that the blood uric acid is definitely increased in gout. This assertion was first made by Alfred B. Garrod, based on observations made in 1847 and 1848. His famous thread test for demonstrating uric acid in blood serum obtained by the application of a blister is well known. He even demonstrated an excess of uric acid in the blood by a quantitative method. With recent quantitative methods the uric acid in gout is generally found

to range between 3 and 10 mg. per 100 cc. of blood It may rise even to higher levels. In a study of 17 typical cases of gout Berglund (1925) found the plasma uric acid to range between 6.5 and 14.7 mg. per 100 cc. In three other doubtful cases the amount ranged between 3.5 and 5.8 mg. In a study of 19 cases of chronic polyarthritis of non-gouty origin he found the values much lower, between 2.2 and 5.8 mg. Five had values below 3 mg. Although the increase in the blood uric acid in gout is generally conceded, it should be stated that Magnus-Levy, Maase, Umber, Gudzent and others have reported gout cases without an increased blood uric acid. Gudzent, writing in 1924, even states that 30 per cent. of his cases of gout have shown a normal amount of uric acid in the blood. One naturally questions the methods of quantitative determination. With the Folin-Wu method, cases of undoubted gout, made certain by the presence of tophi, invariably show an increased blood uric acid. Uricemia is not found in gout alone. It occurs in leukemia, occasionally in pneumonia, and particularly in chronic interstitial nephritis. In the latter disease with uremia Myers and Fine found 27 mg. of uric acid per 100 cc. of blood.

The Excretion of Uric Acid in Gout.—Garrod was the first to claim that there is a diminished excretion of uric acid in gout. He believed that this was true both of the acute attack as well as of chronic gout. Since the adoption of more reliable methods of quantitative analysis in recent years, Garrod's results have not been confirmed *in toto*. Minkowski states that the following conclusions may be drawn: (1) The daily excretion of uric acid, in the intervals between acute attacks, ranges within the same limits as does the excretion in healthy individuals. (2) In chronic gout, even in those cases in which there is marked deposition of urates in the tissues, a constant diminution in excretion of the uric acid has not been definitely proved. (3) Immediately preceding and following an attack there is regularly a diminution in the amount of uric acid eliminated in the urine, whereas during the attack the uric acid output is often markedly increased. The writer, however, has found in some cases of chronic tophaceous gout a marked diminution in the uric acid elimination between acute attacks.

Excretion of Uric Acid in the Urine in Gout.—There seems to be a general concensus of opinion that the uric acid excretion in the urine falls for a day or two previous to an acute attack. This initial drop is followed by a marked rise, reaching a maximum on the second or third day of the seizure, when it may reach normal limits or even above the normal. This has been shown clearly in curves made by Umber in gout patients on a purin-free diet. Many years ago the writer demonstrated similar curves by quantitative methods not so accurate as those now in use. His found that on a mixed diet the uric acid excretion in the intervals between acute attacks was not abnormally low. The writer's determinations, however, frequently showed a marked diminution of the excretion over long intervals between attacks. Schittenhelm and Schmidt found the excretion below normal in 80 per cent. of their cases.

On a mixed diet Hammarsten found that normal persons excreted from 0.4 to 1 gm. of uric acid in the twenty-four hours. From analyses

collected from the literature Pratt found that the average daily excretion of uric acid of twenty normal persons on a purin-free diet was 0.39 gm., while the average daily excretion of 20 gouty patient on a purin-free diet was 0.25 gm. Where gout is associated with plumbism the uric acid excretion is lower than when plumbism does not exist.

Effect on Uric Acid Excretion of Administration of Exogenous Purins.—In gout exogenous purins are excreted less well than in health. It is customary to give the purins in the form of sweet-breads, although the statement holds for any purin. McClure and Pratt have collected 50 observations from the literature. In 32 of these, 20 per cent. or less of the purin nitrogen of the food was excreted as uric acid nitrogen. In 19 tests the excretion of exogenous uric acid nitrogen was 10 per cent. or less. These results were strikingly different from those obtained in health. Among 40 observations on healthy persons, in only 3 was the percentage of exogenous uric acid nitrogen 20 per cent. or less.

Brugsch and Schittenhelm hold that in gout there is not only a diminished but also a delayed excretion of exogenous uric acid, and consider this characteristic of the disease. Although this view has received general acceptance, McClure and Pratt cast doubt on it, for they have found that the excretion of exogenous uric acid may not be completed in healthy persons for three days. The same observers are further of the opinion that the diminished excretion, and delayed output of exogenous uric acid, is valueless in differentiating gout from other forms of arthritis, for they have found the same diminished excretion and delayed output in arthritis deformans.

In 1924 Gudzent published the results of some experiments carried on in association with Wille and Keeser. They injected monosodium urate intravenously into normal and gouty individuals and made frequent simultaneous determinations of the uric acid in the blood and urine. They claim to have obtained the following results. (1) In all cases the monosodium urate rapidly disappeared from the blood into the tissues. In this respect their results were in accord with those obtained by the injection of all other molecular substances. (2) In one group of cases the monosodium urate rapidly reappeared again in the blood, as indicated by the rise in the percentage of blood uric acid and was rapidly excreted by the kidneys. (3) In a second group of cases—the gout cases chiefly—the monosodium urate remained to a greater or lesser extent in the tissues. They term this retention in the tissues "uratohistechie."

Functional Activity of the Kidneys in Gout.—McClure and Pratt, basing their findings on functional kidney tests, are of the opinion that in gout the metabolic disturbances causing the disease lessen the functional activity of the kidneys, even when there are no evidences of nephritis judged by the usual criteria. They found that the phenolsulphonephthalein output was lowered, the specific gravity of the urine fixed, the amount passed at night increased, and that in all cases there was retention of non-protein constituents in the blood.

Theories Concerning Gout.—It must be admitted frankly that, up to the present time, there is no satisfactory explanation for the cause of gout upon which the leading investigators of the disease are in agreement.

Many explanations have been advanced but none of them has been convincing or has withstood the test of time. The whole question seems to remain a matter of speculation. That purin metabolism is markedly disturbed is indicated by the generally accepted view that the uric acid of the blood is increased in gout and by the fact that the outstanding pathological lesion in the disease is the tendency to deposition of urate of soda in cartilage and the periarticular tissues. The tendency has been to attribute the symptoms of the disease to uric acid and its deposition in the structures mentioned. The balance of opinion still favors this conception. Yet there are others who maintain that some still unknown factor exists which causes changes in the tissues which are responsible for the secondary deposition of the urates. A clear explanation of the cause of gout, such as we now possess for diabetes, is still lacking.

The Renal Theory.—The view was advanced by Alfred B. Garrod in 1848 that in acute gout the alkalinity of the blood is diminished and that the uric acid of the blood is increased owing to a deficient power of elimination on the part of the kidneys. He believed that the lessened alkalinity diminished the ability of the blood to hold the uric acid in solution and favored its precipitation in the tissues. His views concerning the lessened alkalinity of the blood have been disproved. His retention-theory on the part of the kidneys still has numerous advocates. Arguments in favor of the retention theory are the low excretion of endogenous uric acid between acute attacks and the high uric acid concentration of the blood. A strong objection to the theory is the fact that during an acute attack the kidneys are capable of excreting large amounts of uric acid.

The Nervous Theory.—In 1784 Cullen advanced the view that gout was primarily due to an affection of the nervous system. In modern times Sir Dyce Duckworth has been the chief supporter of the nervous origin of gout. He has pointed out the influence of depressing conditions, mental and physical, in precipitating acute attacks. This view has few supporters.

Primary Tissue Change Theory.—Ebstein held the view that some change causing primary necrosis of the tissues was necessary before deposition of urate of soda could occur. His work was based on microscopic studies of the tissues. He called attention to the early stages of the necrotic process, in which he found no deposition of urate of soda, the laying down of urates in these areas occurring as a secondary process. The most recent supporter of this view was the late Sir Clifford Allbutt who laid down the axiom "That in gout urates are never deposited in sound tissue, whether cartilage or bone." He based his view on his own investigations, as well as upon the histological studies of gouty tissues by Strangways.

The Ferment Theory.—Brugsch and Schittenhelm maintained that gout is due to a disturbance of the entire series of ferments concerned in the formation and destruction of uric acid. In gout they believed that there was retarded uric acid formation, retarded uric acid destruction, and retarded uric acid elimination. Their elaborate theory was opposed by the work of Wiechowski, who showed that uric acid is not destroyed by

any human organ, and by Jones and his associates, Austrian and Winternitz, who demonstrated that the distribution of the ferments in gout did not differ from that of normal persons.

Tissue Retention Theory.—Umber believes that the tissues in gout possess a special affinity for uric acid. The view presupposes an abnormal chemical property of the tissues which leads to this retention. The view received considerable support from work published by Gudzent, Wille and Keeser, in 1924, who found after intravenous injections of monosodium urate in healthy and gouty patients, that in all cases the uric acid rapidly disappeared from the blood and was deposited in the tissues. In normal persons it was soon liberated again from the tissues and excreted in the urine, while in the gouty patients the monosodium urate remained in the tissues.

Pathological Accentuation of Renal Insensitiveness Theory.—Reference has been made to the work of Folin, Derick and Berglund which led them to explain the high uric acid content of the blood in normal human beings as compared with that of the blood of other mammals on the basis that the human kidney was relatively insensitive to uric acid and consequently did not excrete it as freely as did the kidneys of other mammals. As a result of these and other investigations Berglund in 1925 advanced the theory that the high uric acid content of the blood in gout was dependent upon a pathological accentuation of the renal insensitiveness to uric acid excretion. In a sense it brings us back to Garrod's renal retention theory of 1848.

Concerning the merits of the various theories, the writer is of the opinion that the renal retention theory, although based on inadequate experimental evidence, has more evidence to support it at the present time than any of the others. The view of Berglund, based on the important studies of Folin, Derick, and himself published in 1924, in which he holds that the high uric acid content of the blood in gout is due to a pathological accentuation of the normal insensitiveness of the human kidney to excrete uric acid, tends to support the renal-retention theory. Berglund's view requires further confirmation, however, before it can be accepted.

To the writer the most appealing explanation of the excess of uric acid in the blood is the view that it is dependent on deficient destruction of uric acid, although there is insufficient evidence to prove it. We have seen what an important part the various enzymes play in the intermediary metabolism of the nucleoproteins. So far no investigator has been able to discover that any of the human tissues contain a uric acid destroying enzyme, whose function it is to convert uric acid into allantoin, such as occurs in many animals. Possibly someone may do for gout what Banting has done for diabetes. Should such an enzyme be found, it could help materially to solve many of the mysteries of the gout problem.

Pathology.—Blood. With the Folin and Wu method of quantitatively determining uric acid the blood of patients with undoubted tophaceous gout appears always to show an excess of the acid. Reports of normal blood-uric-acid findings seem to have resulted from the use of less reliable quantitative methods. Normally the blood contains from 1 to 3 mg. of uric acid per 100 cc. In gout the amount ranges from 3 mg. per 100 cc.

upward. Berglund reported a case of gout with 14.7 mg. per 100 cc. of blood plasma.

There is no special tendency to anemia. The leukocytes are not increased except slightly during an acute attack. One of our cases with tophaceous gout died of pernicious anemia. Neusser occasionally found an eosinophilia, and Chalmers Watson has seen numerous degenerated myelocytes during acute attacks. Neusser's so-called "perinuclear basophilic granules," which he considered pathognomonic of a uric acid diathesis, have been shown by the writer and others to be due to artefacts and to occur in the blood of normal individuals with the same technique. There was no association between the excretion of the alloxuric bodies and the relative abundance of these granules, as he supposed. Investigations tend to show that there is no constant reduction in the alkalinity as has been held by Garrod, Haig, and others. In saturnine gout, the red cells are likely to manifest the basophilic granular degeneration seen in lead poisoning.

Joint Changes.—The characteristic lesions of gout manifest themselves particularly in and about the articulations. They are dependent upon the deposition of uric acid in the form of sodium urate, and on the inflammatory and degenerative processes which result therefrom.

In the gouty joint the articular surfaces are found studded with specks, streaks, or patches of white, mortar-like material. This is composed of sodium urate deposited as long acicular crystals. It is likely to be most abundant toward the central portion of the articular surfaces. The sodium urate is not on the surface of the cartilages but is covered over by a thin layer of cartilaginous tissue. It seldom reaches the bone and, as Garrod pointed out, rarely penetrates beyond two-thirds of the depth of the cartilage. In very advanced, chronic cases there may be actual erosion of the cartilage but this is rare as compared with arthritis deformans. In the chronic cases, the urate deposit often invades the capsular tissues, and may even infiltrate the skin, and lead to suppuration of a joint tophus. The urate deposit in the cartilage can be demonstrated microscopically in sections cut at right angles to the articular surface; also by the simpler method of scraping off some of the articular cartilage, teasing in salt solution and examining microscopically. It is believed that the urate is deposited from the synovial fluid of the joint cavity. In the chronic cases there is much thickening of the capsular tissues. In these there may be increased dryness of the joint; but if the patient dies during an acute attack, there is usually, particularly in the knee-joints, an excess of synovial fluid, and the synovial membrane may be reddened and injected. The synovial fluid is usually somewhat turbid, and contains a varying number of polymorphonuclear leukocytes and occasionally acicular crystals of sodium urate.

There is diversity of opinion, regarding the essential cause of the urate deposition. Ebstein insisted on a primary tissue-necrosis. It seems more likely that, if this view be correct, the areas of necrosis result from the toxic action of some as yet unknown poison. These necrotic areas are most liable to occur in the joint cartilages and other cartilaginous and articular structures in which the normal nutritional currents are slow.

In support of his view, he stated that he often found areas in which there was necrosis without urate deposition. In these areas of coagulation necrosis, the reaction is always acid, so that the conditions are favorable for the precipitation of the uric acid in the form of the crystalline urate. Ebstein's view has recently received the support of the late Sir Clifford Allbutt; based in part upon the extensive studies of Strangways, Allbutt believed that in gout the urates are never deposited in sound tissue. Von Noorden thinks this necrosis may be due to a special ferment. His and Mordhorst claim that the deposition of the sodium urate is primary, and that the tissue necrosis is secondary. According to Roberts, the urates are deposited most abundantly in cartilaginous tissue, because here the temperature is lowest, the circulation poorest, and, in the case of the articular cartilage, it is bathed with the synovial fluid, which is rich in sodium chloride, and which he claims favors the deposition of sodium urate. According to Wynne, the marginal outgrowths about the gouty joints are true exostoses. The bursæ may be acutely inflamed and may contain deposits of urate of soda.

The frequency with which urate deposits are found in the joints at autopsy corresponds closely with the relative frequency with which the gouty arthritis is seen clinically. Norman Moore brought this out well in an analysis of 80 autopsies on gout patients. The joints most commonly involved are the metatarsophalangeal joints of the big toes, and frequently these are the only ones affected. Then follow the tarsal joints, ankles, knees, hands, and wrists. The elbows, shoulders, and hips are more rarely involved. Among the rarest sites are the articulations of the jaws, larynx, and sternoclavicular joints.

Situations in which Tophi Occur.—Urate deposits occur in other situations than in the joints and their neighborhood. These are termed "tophi," a name derived from the Hebrew, and signifying "concretions." They are also known as "chalk-stones." The commonest situation is on the helix or anti-helix of the ear. They are also frequently found in the tendons and aponeuroses. In 1 case the writer saw a tophus measuring 3 by 6 cm., in the tendo Achillis. They are not infrequent in the subcutaneous tissue. The commonest seats of skin tophi are the extensor surfaces of the forearms, near the elbow-joint, and the neighborhood of the patella. They may be mistaken for rheumatic subcutaneous nodules. Enormous deposits may occur in the olecranon and prepatellar bursæ. The writer observed a patient with numerous tophi in the prepuce; another had a large group of them over the sacrum. They may also occur in the palms and soles, nose, and tarsal cartilages of the eyes. Less common situations are the laryngeal cartilages, vocal cords, cranial and spinal dura mater, the pia mater, sclerotic coat of the eye, the fibrous sheaths of the nerve trunks, and the aortic valves. Enormous tophi, which may break down and suppurate, not infrequently occur about the finger- and knuckle-joints. Ebstein and Sprague analyzed the tophi, and find that they contain, on an average, 57 per cent. of sodium urate and from 12 or 13 per cent. of calcium urate. Somewhat similar to these tophi in man are the deposits characterizing "guanin gout" in hogs.

When these animals are fed in a certain way, one sees in the muscles, ligaments, and articular tissues, small whitish deposits of guanin.

Kidneys.—Of the visceral lesions, those of the kidneys are the most frequent and important. Nephritis is extremely common, and, according to Levison, is always present. Ebstein described two types of gout cases: (1) the "primary renal gout," and (2) the "primary articular gout." In the former, the renal disease exists for some time, and, subsequently, articular manifestations of gout appear. A colored man, aged twenty-four years, admitted to the Johns Hopkins Hospital, for several months had complained of the usual symptoms of chronic nephritis without any previous arthritic history. A few days before his death, he developed pain and swelling of his right big toe-joint. This joint at autopsy showed the characteristic deposits of sodium urate in the articular cartilage. The kidneys were much contracted. In the latter type, the articular manifestations antedate the onset of the clinical symptoms of nephritis. The form of nephritis usually met with in gout is that characterized by granular degeneration and marked atrophy. It is often spoken of as the "gouty kidney." On the other hand, the arteriosclerotic kidney may be met with. Here the kidney is larger, beefy, red, and very hard. There appears to be no special difference between the kidney of saturnine and that of ordinary gout. The gouty kidney, on section, not infrequently shows white deposits of sodium urate. In the cortical substances the deposit is scanty and occurs in specks scattered irregularly through the tissue. It is, however, most frequently seen, and most abundant, in the pyramids, occurring in streaks running in the direction of the tubules particularly toward the apices of the pyramids. In both situations, the deposit is usually situated in the intertubular tissue, but it may also occur in the lumen of the tubules. When examined microscopically it is seen to exist as acicular crystals, just as in the gouty joints. They are not so frequently found as we would be at first led to infer. Norman Moore found them in only 12 of 80 cases. Osler held that these deposits must not, however, be always interpreted as meaning that the individual has gout, as they occasionally occur without the person having had any gouty manifestations.

Cardiovascular Lesions.—Arteriosclerosis is very common. Nearly all cases of chronic gout show marked thickening of the peripheral arteries. Whether the arterial thickening is due to the toxic action of the excess of uric acid in the blood, to that of the products of intermediary metabolism, or to the contributory factors producing the gout—viz., alcohol, lead, or excessive food—is difficult to determine.

The combination of nephritis and arteriosclerosis with consequent hypertension often leads to hypertrophy of the left ventricle. The arch of the aorta is frequently involved in the arteriosclerotic process. The orifices of the coronaries may be narrowed and the coronary vessels sclerosed. Myocardial changes are common, and death may result from failure of compensation. A gouty pericarditis is not uncommon. In rare instances, sodium urate deposits have been found in the aortic valves.

Respiratory System.—Sodium urate deposits may occur in the vocal cords, and in the epiglottis and laryngeal cartilages. In rare instances

the urate crystals have been found in the sputum. Emphysema is very common in chronic gout, and there may be a chronic bronchitis.

Symptoms.—Acute Gout.- In the initial attack there may be no premonitory symptoms. A previously healthy man of middle age retires feeling perfectly well. During the night he is awakened with intense pain, usually in the right metatarsophalangeal joint. By morning the joint is reddened, slightly swollen, and sensitive to the touch. The temperature is moderately elevated, reaching usually to between 101° and 103° F. As morning approaches, the pain, which has been agonizing and makes the patient feel as though the joint is being squeezed in a vise, gradually subsides, and, beyond having a feeling of general malaise and of anorexia, he experiences a fairly comfortable day. The next night the attacks recurs, and the pain, as Sydenham says, "insinuates itself with the most exquisite cruelty among the numerous small bones of the tarsus and metatarsus, in the ligaments of which it is lurking." There is a repetition of these attacks each night for a week or ten days, constituting a so-called "fit of the gout." For the first few days the swelling of the joint increases, coincident with which there is a gradual abatement of the intensity of the pain. The skin over the joint is reddened and shiny. The surrounding veins are slightly dilated, and, toward the end of the attack, there may be slight pitting on pressure over the joint. The inflammation never goes on to suppuration. With the subsidence of the acute swelling, the skin may desquamate. During the acute febrile period, there is a leukocytosis which may reach 20,000 per cmm. In the initial seizure both big toe-joints may be involved. On the other hand, these articulations may escape, and the tarsal and tarsometatarsal joints may be first affected. In these instances the "fit" generally lasts considerably longer. After the attack, the general health may be decidedly improved. There may be no recurrence of the acute attack for years. More commonly, however, only months elapse, and there is a tendency to periodical recurrences in the spring and fall. Premonitory symptoms occasionally precede the acute attacks for a number of days, and the victim can often predict its onset. These symptoms are quite diverse. The most prominent ones are digestive disturbances -loss of appetite, flatulence, and acidity. Nocturnal restlessness, irritability of temper, and depression of spirits may also occur.

Chronic Gout.—With the progress of the disease, the acute exacerbations become more frequent and a larger number of joints become affected. The tarsal, ankle, knee, hand, and wrist-joints are the ones most likely to be involved, in the order of frequency mentioned. The elbows, shoulders, and hips are more rarely attacked. The periarticular tissues become thickened, and densely infiltrated with urates. The latter, particularly about the toe, knee, finger, and elbow-joints, may give rise to large joint-tophi, which, in the case of the knee and elbow-joints, may reach the size of a walnut. These tophi may cause striking knob-like deformities of the knuckle and interphalangeal articulations. They gradually become superficial, and appear whitish through the superimposed skin. The latter, especially over the knuckle and metatarsophalangeal joints, may become inflamed and actually ulcerate, and

the contents of the tophi discharge as a whitish, chalky material, which, on microscopic examination, reveals the characteristic needle-shaped crystals of sodium urate. In these cases of chronic "tophaceous" gout, the commonest situation for the tophi is the cartilage of the ear, in the region of the helix and antihelix. They appear first as slight reddish elevations in which, as time goes on, the urate can be recognized with the naked eye as a whitish "chalk-stone like" deposit. The term "chalk-stone" is not altogether a misnomer, for Ebstein and Sprague have shown that tophi contain from 12 to 13 per cent. of calcium urate, although the greater portion, 57 per cent., is composed of sodium urate. Subcutaneous tophi may occur about the knees and along the extensor surfaces of the forearms, and may be mistaken for fibroid nodules. They may also occur in the palms, and soles, and over the sacrum, and in the tendo Achillis. Tophi sometimes occur in the tarsal cartilages of the eye, in the sclerotics, and in the cartilage of the nose. The bursæ over the olecranon and patella may become inflamed and be the seat of sodium urate deposition. Polyarticular attacks, with moderate fever reaching 101° F. occur with frequency, and in the intervals the unfortunate victim is not entirely free from pain, and always conscious of joint disability. Owing to the lessened amount of synovial fluid in these chronic cases, audible creaking of the joints may occur, and there is sometimes palpable crepitation. The acute joint exacerbations may be afebrile, a feature which should always lead the physician to suspect a gouty origin for the joint symptoms. The pulse tension is increased, the peripheral arteries become sclerosed, and hypertrophy of the left ventricle develops. Cramps of the calf, abdominal, and thoracic muscles may be most annoying. Digestive disturbances are common. The victim of chronic gout may possess marked mental and bodily vigor. Certain of the most distinguished members of our profession have been martyrs to the disease, notably the elder Scaliger, Jerome Cardan, and Sydenham, whose statement that "more wise men than fools are victims of the affection" still holds good. Although the subject of chronic gout is liable to be carried off by some terminal affection such as uremia, pleurisy, pericarditis, peritonitis, and meningitis, yet the victims not infrequently live to a good old age. The question has been much discussed as to whether Heberden's nodes ever occur in gout. Although of rare occurrence, it seems quite certain that they do occur, for Charcot, Duckworth, and Minkowski, have described them in cases of unquestioned gout. Dupuytren's contraction of the palmar fascia has been described.

Irregular Gout.—This comprises a nondescript group of symptoms which have usually been embraced under the terms *lithemia*, or a *uric acid*, *lithic acid*, or *gouty diathesis*. These irregular features are observed in members of gouty families who may never have suffered from an attack of gouty arthritis. They occur, also, in those who have eaten and drunk too freely, without taking sufficient exercise, and who have been fortunate enough to escape an acute attack. In families with marked hereditary predisposition, the daughters often escape, while one son may have gouty attacks of great severity even though he lives

a temperate life and endeavors to avoid the conditions favoring the disorder. Another son, on the other hand, has only the irregular features, and never the acute articular affection. While the irregular manifestations are more likely to occur in inherited gout, they may also occur in the acquired form. There is an unfortunate tendency on the part of many physicians to ascribe certain obscure symptoms to a so-called uric-acid diathesis, especially if they find a deposit of uric acid or urates in the urine, although there is often not a vestige of evidence to justify this view. There are certain health resorts in this country from which nearly every patient comes away imbued with the firm conviction that his blood is "filled with uric acid," and that this is responsible for his various nervous features. The patients are usually pleased with the explanation, and it is a difficult task to disabuse their minds of the fallacy. Among the commonest manifestations of irregular gout are the following:

(*a*) *Cutaneous Eruptions.*—The most distinctive is eczema. The favorite seat is the external ear, but the inflammation may spread to the face, forehead, and back of the neck. It may be very obstinate, and even extend to other parts of the body in patients of advanced years. Symmetrical patches of psoriasis may occur on the legs. Attacks of herpes zoster have occasionally occurred. The nails are often striated and fluted, or lined vertically.

(*b*) *Alimentary Disorders.*—There may be psoriasis of the tongue. Notwithstanding numerous statements to the contrary, Duckworth asserts that no uratic deposits are met with in connection with the jaws, teeth, or gums. It has been held by some that the development of tartar on the teeth is a gouty manifestation. There seems no justification for this view. Some patients are subject to frequently recurring attacks of pharyngitis with great injection of the vessels. A gouty parotitis occasionally occurs. Attacks of what is termed biliousness, in which the tongue is furred, the breath foul, the bowels constipated, and the action of the liver torpid, are not uncommon in gouty persons.

(*c*) *Nervous Manifestations.*—Some of the most frequent manifestations of irregular gout come under this heading. Headaches and migraine attacks are common. Neuralgias are not uncommon. Sciatica is believed frequently to have a gouty basis. Duckworth has emphasized the occurrence of hot or itching feet at night. Plutarch mentions that Strabo called this symptom "the lisping of the gout." Cramps in the leg and abdominal muscles may be troublesome.

(*d*) *Urinary Disturbances.*—Many fallacious opinions have been formed by physicians concluding that a person is suffering from a uric acid diathesis by finding deposits of uric acid and urates in the urine. The solubility of the latter is dependent upon so many factors, important among them being the amount of urinary pigment and the percentage of the various salts, that it is entirely unjustifiable to draw any definite conclusions as to the quantity of uric acid excreted without making quantitative analyses. Uric acid precipitation may occur, although there may be actual diminution in the uric acid excretion in the twenty-four hours. Individuals with a gouty habit are undoubtedly prone to gravel, and to uric-acid calculi. Duckworth points out that articular

gout and calculi rarely coexist although they may alternate. Albuminuria is very common in the gouty dyscrasias. Oxaluria also occurs. Hematuria may occur in very old persons. Phosphatic gout has been described. It occurs without the articular features. Severe pain comes on in the night and there is spasmodic dysuria. Urethritis, with a purulent discharge, is said to occur either spontaneously or following a pure connection.

(*e*) *Ocular Manifestations.*—Hutchinson called attention to hot and itching eyeballs as a frequent sign of masked gout. Associated or alternating with this symptom there may be attacks of episcleral congestion. The writer observed repeated attacks of unilateral conjunctivitis in a gouty patient, who for years had no articular symptoms. These would occur with, or independently of, a gouty pharyngitis.

(*f*) *Cardiac Manifestations.*—A peculiar paroxysmal disturbance of the circulation is sometimes witnessed, in which the heart-rate is very rapid. There may be attacks of cardiac pain without manifestations of cardiac disease.

(*g*) *Pulmonary Features.*—Greenhow has pointed out that persons of the gouty habit are liable to suffer from chronic bronchitis. Asthmatic paroxysms may also occur. The prevalence of emphysema is well recognized.

Urine.—During the acute paroxysms the urine is scanty, high colored, and is generally stated to contain a deposit either of urates or uric acid. In the writer's experience such a deposit is the exception rather than the rule. There is usually a trace of albumin with a few hyaline or granular casts and there may be a mild glycosuria. Quantitative analyses always show a marked reduction in the amount of uric acid below the usual level for two or three days before the acute attack. Twenty-four or forty-eight hours after the onset of the acute symptoms the uric acid curve rises, and the amount may reach 0.7 to 1 gm., the upper limit for normal. As the acute symptoms subside, the curve falls to 0.4 gm., the lower limit for normal, or usually below this. In chronic gout, the urine is usually increased in quantity, pale, of low specific gravity, and always contains traces of albumin and hyaline and granular casts. Although some have failed to find a constant reduction of uric acid in the intervals between the acute attacks in these cases, the writer's analyses have practically always shown a very marked reduction, often not more than 0.1 or 0.2 gm. being excreted in the twenty-four hours. In 1 or 2 cases, he has failed to find, on certain days, any precipitation of uric acid as ammonium urate, with Folin's modification of the Hopkins quantitative method. Many hold that there is no corresponding increase in the excretion of the phosphoric acid with that of the uric acid during the acute attacks, but, in some of the cases followed, the writer found a striking parallelism in the curves of the two acids. If the uric acid be derived from nuclein destruction a correspondence in the curves would rather be expected.

Complications.—Cardiovascular.—Arteriosclerosis is extremely common and, owing to the increased tension, hypertrophy of the left ventricle occurs. In due time myocardial insufficiency appears and myocarditis is common in the obese cases. This is probably induced by the changes in the coronary arteries, and may be the eventual cause of death. A ter-

minal pericarditis is not uncommon but this is usually attributed to the renal lesion rather than directly to the gout. Aneurism and apoplexy may occur. Phlebitis and venous thrombosis are well recognized as occasionally of gouty origin. The French are inclined to the view that many instances of so-called idiopathic thrombosis of the veins are due to a gouty dyscrasia.

Renal.—A chronic interstitial nephritis, and small granular kidneys, are almost invariably present in the chronic form of the disease, and the majority of gout patients die of uremia. Calculi may occur.

Retrocedent Gout.—This term is applied to a group of serious internal symptoms, occurring coincidently with a rapid disappearance, or improvement, of the joint manifestations. They may be so grave as to cause death, and may be considered among the complications. With a sudden cessation of the arthritis there may be severe gastro-intestinal symptoms —pain, vomiting, diarrhœa with great depression, and death may occur during such an attack. Or there may be cardiac manifestations—dyspnœa, precordial pain, and irregular heart action. Cerebral features, such as delirium, coma, or apoplexy, may occur, but in a majority of cases these symptoms are probably uremic. The writer has never observed a case of retrocedent gout.

Of the *eye* complications, an iritis is recognized as being of gouty origin. Glaucoma occurs, Hutchinson described a hemorrhagic retinitis. This may be of renal origin, but it is especially characterized by being unilateral, and affecting the left eye most frequently. A suppurative panophthalmitis has been described.

Glycosuria and Diabetes.—Although certain observers refer to the comparative frequency of glycosuria in gout, the writer has rarely observed it. It occurs, usually, in the obese gout patients. The glycosuria may alternate with arthritic manifestation (diabetes alternans). Lecorché observed 23 cases of transitory or permanent glycosuria in 150 cases of gout. We now know that the glycosuria must be dependent upon insufficiency of the internal secretion of the islands of Langerhans. How this insufficiency is caused in gout is unexplained. Gout patients are often obese and obesity predisposes to a lowering of carbohydrate tolerance.

Diagnosis.—In the majority of cases of the acute form no great difficulty should arise. The predilection for the local inflammation to attack the metatarsophalangeal joint of the great toe and the tarsal joints is very characteristic. The marked reddening and the shiny appearance of the skin, with the intensity of the pain, are extremely suggestive. Before the disease has definitely reached the chronic stage the joint inflammation may be polyarticular, and many of these cases are diagnosed as rheumatic fever. Careful inquiry regarding heredity, habits as to eating and drinking, together with the occupation, will often give the proper clue. The examination of the blood for an excess of uric acid is of value.

Quantitative determinations of the uric acid in the urine help us little, unless one is able to follow the curve, before, during and after an acute attack. A valuable procedure is the quantitative estimation of the uric acid in the urine, first on a purin-free diet and then after the addition of a known quantity of purin to the diet. In a normal individual when

some purin food is added, such as a weighed amount of sweet-bread, the excretion of the added purin is prompt, and is completed in two days; the gouty individual shows a delayed excretion of such added purin, the increased elimination of uric acid continuing from three to five days.

It is in the chronic form, with occasional acute exacerbations, that the correct nature of the arthritis is often overlooked. This is particularly the case if tophi have not yet appeared; but many cases go begging for a diagnosis even when these are present, owing to the failure of the physician to search regularly for tophi in the ears in all cases of acute or chronic joint affections. The tophi are commonest in the cartilaginous portions of the ear in the vicinity of the helix and antihelix. They are usually small, superficial, and whitish in appearance. They may be more deeply seated and the urate deposits may not be seen with the naked eye. Microscopic examination of the contents shows the characteristic needle-shaped, acicular crystals of sodium urate. The presence of these crystals is pathognomonic of gout. Not to be confused with the tophi, are Woolner's tip or the Darwinian tubercle, which is more developed in some than in others, small fibroid nodules on the margin of the ear, and small sebaceous cysts. The latter is the only one to give rise to any real confusion, and the finding of oil droplets and epithelial cells, with the absence of urate crystals in the contents, easily differentiates the two. Where there are large urate accumulations about the toe, finger, knee, or elbow-joints, the diagnosis is manifest at first sight. It must be recalled that subcutaneous tophi, clinically indistinguishable from fibroid nodules, may occur over the extensor surfaces of the forearms and about the knees, and may seem confirmatory of rheumatism. It is well in any such doubtful cases to excise one of these nodules and examine microscopically. The presence of sodium urate deposits points definitely to gout. A feature of diagnostic importance is the fact that an attack of acute gouty arthritis may be afebrile. Any polyarthritis, with acute manifestations and unaccompanied by fever, should always cause a strong suspicion that it is gouty in origin. In these chronic cases, the habits of life and the history of the situations of the initial attack of arthritis are most important. If there be an arthritic family history, if the patient has indulged freely in fermented beverages, or has had an occupation subjecting him to possible lead infection, and if the initial or early attacks have been limited to the metatarsophalangeal or tarsal joints, the chances are strongly in favor of the disease being gout.

Opinion varies as to the value of the *roentgen-rays* in the diagnosis of gout. The so-called "punched-out" areas in the bones have been considered as characteristic. These areas are believed to represent existing deposits of urate of soda, or areas from which the urates have been absorbed. Urate deposits in bone are supposed to offer less resistance to the roentgen-rays and consequently defects in the bones appear in the roentgen-ray plates. We have been inclined at the Johns Hopkins Hospital to place considerable value on these "punched-out" areas in the diagnosis of gout from other forms of arthritis. Pratt, on the contrary, holds that roentgen-rays are of very little value in the diagnosis of gout,

stating that they occur in other forms of arthritis, and are not pathognomonic of gout.

As our knowlege of chronic arthritis has increased, the opinion is more firmly established that there is no such condition as "chronic articular rheumatism." An acute rheumatic arthritis, when it subsides, practically never leaves any deformity or limitation in functional activity. Consequently, when deformity or impaired motion supervenes upon one or more attacks of acute arthritis, we can be reasonably certain that we are not dealing with rheumatic fever but rather with gout or arthritis deformans. It is with the latter affection that the greatest difficulty in the differential diagnosis is likely to occur. In *arthritis deformans* certain features aid in differentiation. In the deformities of the hands, there is a greater tendency to ulnar deflection of the fingers. A most important point is the almost constant occurrence of atrophy of the dorsal interossei muscles of the hands, producing a depressed appearance over the metacarpal region. Heberden's nodes point toward arthritis deformans, although they have been in rare instances described in cases of undoubted gout. The tendency of the laity, and also of many physicians, is to incorrectly consider these enlargements of the terminal finger-joints as a manifestation of gout. When the larger joints are involved in arthritis deformans, such as the knee, wrist, or elbow, the deformity is more likely to be of a fusiform shape with considerable muscular atrophy above and below. Needless to say, tophi do not occur in this disease. The roentgen-rays are of value in differentiating the two affections when actual joint deformity has occurred. Osteophytic growths, or atrophy of the ends of the bones and of the joint surfaces, point respectively to the hypertrophic and atrophic forms of arthritis deformans. It should be recalled, however, that Wynne has described bony outgrowths about the joints in gout. The joint distortions of arthritis deformans are very common in women while those of gout are rare. The term "rheumatic gout" should be abandoned. The disease for which it stands has nothing to do with gout and should be called arthritis deformans.

A chronic arthritis, accompanied by marked arteriosclerosis and the signs of chronic interstitial nephritis, should strongly suggest gout.

The diagnosis of the *irregular forms* of gout in which there have been no articular manifestations, often presents great difficulty and is subject to much uncertainty. The existence of a family history of gout is very important in arriving at the basal cause in these cases.

The writer's personal conviction is that gout in this country is much more prevalent than is generally supposed. Many cases of the acute, and particularly of the chronic, form are mistaken for rheumatism, owing to the failure of the physician to ascertain the family history, the patient's habits, the history of the early arthritic attacks, and to search for evidences of tophi in the ears or elsewhere. It is important to enter a protest against the tendency in certain quarters to ascribe nearly every obscure symptom, usually those of nervous or gastric origin, to a gouty diathesis. The idea that migraine attacks, accompanied though they may be by a precipitation of uric acid or urates in the urine, are due to uric acid dyscrasia, is based on evidence that is far from convincing.

Prognosis.—Once manifestations of gout have made their appearance, they are likely to recur at intervals throughout subsequent life. It occasionally happens, however, that a patient, who in earlier years has been subject to recurring attacks of arthritis, may never show any manifestations after the fiftieth or sixtieth year. This may, in part, be a result of treatment, particularly as regards the habits of living, but it occasionally occurs spontaneously, without the aid of therapeutic measures, which should make us conservative in drawing conclusions regarding the effect of any line of treatment. A fatal termination is unusual in the acute stages although it may occur from the severity of the symptoms resulting from retrocedent or "metastatic" gout. The duration of life is not likely to be materially shortened, so long as the disease maintains its regular character with distinct arthritic manifestations. Often when these appear to play a much less prominent part, visceral complications are likely to arise which may hasten the patient's death. The fatal termination in chronic gout cases is usually due to uremia, myocarditis with dilatation of the heart or to pericarditis. The victims of regular gout often live to an advanced age.

Treatment.—Until we know with positive certainty the actual basal cause for gout, the treatment must necessarily be largely empirical. There is a steadily growing belief that the symptoms of gout are not directly traceable to the action of uric acid. The pathological findings indicate, however, that uric acid and its salts play a conspicuous part in the lesions. The various therapeutic measures have been directed mainly toward influencing purin metabolism, and particularly with the object in view of reducing the excess of uric acid in the blood. It is conceivable that this reduction may be brought about in one or more of the following ways: (1) diminishing the formation of uric acid; (2) increasing its elimination; (3) increasing the rapidity of its oxidation in the body; (4) increasing its solubility in the blood and tissue juices.

Prophylaxis in Members of Gouty Families.—In families in which there is a marked history of hereditary gout, something may be done to lessen the liability of individual members to develop active manifestations of the disease. By temperate living, abstaining from alcohol, and eating moderately, the risks are materially diminished. An active outdoor life, with plenty of exercise and regular hours, will do much to keep an inborn tendency to the disease in abeyance.

The treatment of the disease after actual manifestations have made their appearance may be discussed under various headings: hygienic, dietetic, alkalis and mineral waters, local measures, medicinal, operative treatment, and treatment of the complications.

Hygienic.—Gout prevails chiefly among well-to-do individuals who are not forced to make a livelihood by following occupations requiring even the average amount of physical exercise. Many manifest a tendency to obesity and lead sedentary lives. It is most important in these persons to encourage a more active outdoor life requiring physical exercise in moderation. This must not be overdone, and must be confined within the limits of fatigue, for an acute attack may be precipitated by excessive physical exertion. The patient should be encouraged to do a certain

amount of walking each day, and a particularly useful exercise is horse-back-riding, owing to its beneficial effect on the intestinal functions. Golf can be highly recommended. As an adjunct, certain gymnastics may be prescribed with advantage, such as the use of dumb-bells, Indian clubs, and the various forms of resistance movements. Massage increases the muscular tone, stimulate the circulation, and tends to improve the general metabolic functions. The skin functions should be increased by systematic bathing. In the sthenic cases, cold baths may be used, and, when there is a tendency to obesity, with no contra-indications in the way of myocardial disease, an occasional Turkish bath may be taken with advantage. The bowels should be carefully regulated. The patients should dress warmly, avoid rapid changes in temperature, and be careful not to have the skin suddenly chilled.

Dietetic.—The regulation of the food is undoubtedly the most important factor. Meat is the article supposed to possess the most baneful influence and over which there has been the most discussion. The red meats have for a long time been considered much more injurious than the white meats and fish but there is very little difference between the two so far as the purin content is concerned. Von Noorden and Umber recommend the determination of the purin tolerance of each individual by giving, after several days of purin-free diet, a definite quantity of meat and noting how promptly the individual eliminates this purin. As much purin as the individual has demonstrated himself capable of caring for may be allowed. Umber, according to the delay in excretion, gives from one to six purin fast days each week to allow complete freeing of the system of excess of purins. This he continues for years and, since uric acid retention is greatest at night, he advocates giving what purin is permitted early in the day. In undoubted cases of gout, meats should be given in very small portions only once a day, and from time to time the patient should be put on a purin-free diet for several successive days.

In determining the patient's tolerance for purins the following "Purin-free Test-diet," as suggested by Barker, may be given.

Breakfast: Fruit, 250 gm. (8 oz.); milk, 250 cc. (8 oz.); one roll.

Dinner: Pudding, consisting of 100 gm. ($3\frac{1}{2}$ oz.) wheat flour, 150 cc. (5 oz.) milk, 3 eggs, and 50 gm. ($1\frac{2}{3}$ oz.) butter; 200 gm. ($6\frac{1}{2}$ oz.) stewed fruit.

Supper: Cereal, 50 gm. ($1\frac{2}{3}$ oz.) of meal, 750 cc. (25 oz.) of milk, 20 gm. ($\frac{2}{3}$ oz.) sugar; fruit (raw or stewed) 250 gm. (8 oz.); one roll; butter 50 gm. ($1\frac{2}{3}$ oz.). A liter of water should also be taken in the twenty-four hours.

The patient goes on this diet for three days; the daily excretion of endogenous uric acid is determined quantitatively. Then a weighed amount of meat is given, say 150 gm. (5 oz.). The uric acid is then determined quantitatively each day to ascertain how long it takes for the uric acid to return to the level found to exist during the purin-free test-diet period. Normally the purin of the meat is excreted in one or two days. If in the gout case the total excretion of the purins of the meat requires five or six days, then it is indicated that the purins of the food should be entirely excluded for a considerable period.

During an acute attack of gout the patient should for a day or two go on almost a starvation diet. During this period he should drink water freely. Barley water and weak lemonade may be permitted. After the second day a little bread or toast, milk, gruel, arrowroot, sago or tapioca may be added to the diet. Still later an egg or two daily may be allowed. No purin containing food should be allowed for several weeks.

The protein foods considered particularly injurious, are those rich in cell nuclei and, consequently, containing an abundance of purin bodies. These comprise the thymus, pancreas, liver, kidney, and brain. The meat extracts are to be avoided, owing to their richness in nitrogenous extractives and salt. Straus and Eitner found that the uric acid excretion was increased one to one and a half times after the giving of 50 gm.—a very large dose—of Liebig's meat extract. Fresh fish may be permitted in moderation, but, weight for weight, it has been shown that they cause just as large a uric acid output as do meats. Salt fish should be avoided. Fish roe and caviar should be forbidden, owing to their richness in nuclein, although in the latter it is in the form of paranuclein.

Eggs constitute the most valuable protein food for gout patients, in that they are free from purin bodies. Milk, for the same reason, is also most useful. There is no scientific basis for the belief that cheese should be excluded as casein does not cause an increase in the uric acid excretion. Cheese may therefore be permitted in moderation.

Starchy foods may be freely allowed. An exclusive starch and vegetable diet still, has its advocates but their number is gradually diminishing. Bread, rice, potatoes and other garden vegetables may form a liberal portion of the dietary. Cucumbers and tomatoes are better avoided. In Germany, particularly, the vegetable albumins have been used as a protein food, and as a partial substitute for bread in gout. Of these, aleuronat and roborat have been most extensively used. Certain vegetables, relatively rich in purins, should be excluded; among these are beans, peas, mushrooms, asparagus and onions.

Until recent years the prevailing belief has been that fruits were harmful. It was thought that the acids contained in the fruits were injurious but the acid combinations in the fruits are oxidized in the system into carbonates and consequently fruit must be considered an alkaline nourishment. The best opinion at the present day favors the free use of fruits. The experience in any individual case is the best teacher in this regard, for certain fruits, such as bananas and strawberries, particularly the latter, may excite joint pains, and cause pharyngeal symptoms.

Fats, in the form of butter particularly, may be allowed with freedom; and butter in large quantities was advocated by Ebstein.

All highly seasoned foods should be forbidden. Pepper, paprika, and mustard should not be permitted in dressings. Their only injurious effect is through impairment of the digestive functions. Vinegar should be avoided. Sir William Roberts, who maintained that the sodium salts are injurious, in that they diminish the solubility of the urates and favor their deposition, advises strongly against the use of sodium chloride in the food. He recommended potassium chloride as a substitute.

The most diverse views have prevailed concerning the proper diet and

no set rules can be laid down. The diet in each individual case must be carefully considered. In general terms it may be said that the protein foods, particularly those rich in nuclein or purin derivatives, should be limited but not excluded. The general conviction at the present day is that quantity plays a more important part than quality. The duty of the physician is to see that the patient does not overeat, and to keep his digestive functions in the best possible condition.

The majority of gout patients are better without any alcohol. Individual experience soon teaches the victim that his general health is better and that he is freer from attacks by totally abstaining from alcohol. The fermented beverages are most liable to occasion a lighting up of the arthritic manifestations. The mere indulgence in a glass of beer or wine not infrequently excites in a few hours, or even minutes, twinges of pain in the joints. When alcohol is indicated, as it sometimes is in the asthenic cases, whisky or brandy may be prescribed and does least harm. The richer wines, such as port, sherry, Madeira, champagne, and Burgundy, and strong ales and stout, are very likely to provoke symptoms. In Germany and England, there is a tendency to greater leniency in the use of wine, and the lighter forms are permitted in moderation.

The general advice is that tea and coffee should be eliminated from the diet owing to the methylxanthins they contain.

The gout patient should be induced to drink freely of water, particularly on an empty stomach early in the morning and before the various meals. There is no positive proof that the drinking of water itself causes any material increase in the uric acid elimination, but experience has proved the beneficial effect of the procedure.

Alkalis and Mineral Waters.—Since Garrod advocated the use of lithium carbonate in the treatment of gout, the administration of alkalis has been a popular procedure until recent years. Potassium acetate and citrate have been used extensively. The potassium salts were considered preferable to the sodium salts. The present view, however, is that all alkalis are more harmful than beneficial and have been pretty generally abandoned. Sir William Roberts claimed to have observed fresh attacks of gout apparently brought on by drinking alkaline waters. Van Logheim offered a reasonable explanation for the injurious action of alkalies and the apparent beneficial effect of mineral acids. He injected uric acid subcutaneously into rabbits. He found that the administration of hydrochloric acid per os hindered the deposit of urates and the local inflammatory reaction, whereas large doses of alkalis hastened the formation of tophi. His results have been confirmed by Pfeiffer and Silbergleit. The fact that the acids of fruits yield alkalies in the system might, for the above reason, be considered injurious in gout. Falkenstein advocated the use of large doses of hydrochloric acid. It would be wise to administer 1 to 2 cc. (15 to 30 ♏) of dilute HCl three times daily after meals in patients on an alkaline diet.

Mineral waters have always played an important part in the treatment of gout. All forms may be said to be beneficial, but the good effects are due more to the water than to the contained salts. As Osler says, "Much

of the humbuggery of the profession still lingers about mineral waters, more particularly about the so-called lithia waters."

The mineral springs best suited for gouty patients in this country are those of Saratoga, Bedford, and White Sulphur; in England, Buxton, Bath, and Strathpeffer; in France, Aix-les-Bains and Contrexéville; in Germany, the Sauerling spring of Carlsbad, Wildbad, and Homburg. The drinking of water at home in large quantities, and on an empty stomach, is beneficial but not so much so as at one of these springs, where the accessories to the "cure" mean so much. It is now claimed for these spas that much of their efficiency is due to the radio-activity of the water. The modified diet, freedom from business worries and cares, regular hours, proper exercise, baths, douches, etc., are important adjuncts.

A considerable literature has grown up concerning the *radium* treatment of gout. It was highly recommended by His and his pupils. It was supposed to be most effective as radium emanations. The writer has never observed any beneficial effect from emanations or by the drinking of freshly charged radio-active waters. Fine and Chase failed to find that radium therapy increased the output of uric acid in the urine.

Local Management of the Acute Attack.—The patient should be kept in bed, where he is usually quite willing to remain, owing to the severity of the pain. A mild saline laxative should be administered at the outset. The affected joint, when conditions permit, as in the case of that of the big toe, should be elevated, and wrapped in thick layers of raw cotton surrounded by oiled silk. The use of warm or cold applications locally must depend entirely upon the relative relief experienced in any individual case. Local anodynes may be tried when the pain is severe. A lotion of laudanum and water in various proportions may be applied. Whisky and water, applied quite warm, is a favorite remedy. Ichthyol and lanolin, 10 gr. to the ounce, may be tried. Blisters and counter-irritation by the use of the cautery are rather to be avoided, although the latter may give some relief. Some claim that an attack may be much shortened by beginning early to induce motion of the joint by either active or passive means. Few subjects are willing, however, to consent to such heroic measures. Baking in the dry oven may ameliorate the pain. It is worth while to try the effect of passive hyperemia, which in certain instances has given relief.

Medicinal Treatment.—*Colchicum* is the drug most likely to give relief from the pain. This is so prompt in many instances that it is often referred to as a specific. The drug may be administered either as the wine or the tincture of the seeds, preferably the former, in 20 minim (1.3 cc.) doses every two hours for 4 doses, and then every four hours until the pain is relieved, unless untoward effects manifest themselves. The relief to the pain is usually prompt, but how it is effected is not well understood. It must be discontinued on alleviation of the pain because it is not known to have any direct action on the gouty process. Its active principle, colchicin, is also in use. It is available in granules, each containing 1 mg. In an acute attack four tablets a day two to three hours apart may be given. The administration of colchicum may be abused and harm done. When given in excess, it causes vomiting, purgation, and cardiac depression.

Colchicum sometimes fails to give relief and the salicylic acid preparations may be tried. Although not so likely to give early relief to the pain, yet the salicylates are held in high repute by some clinicians. They increase the total output of nitrogen and materially augment the excretion of uric acid. It is not agreed, however, that their beneficial effect is due to this action. They may be given as sodium salicylate, oil of gaultheria, or acetylsalicylic acid. The last has gained favor, and has the advantage over the ordinary salicylates in being less injurious to the stomach. It may be given in 10 to 20 gr. (gm. 0.6 to 1.3) doses every two or four hours, until pain is relieved.

Antipyrine or phenacetine may be tried for the pain but must be used with caution. In certain cases when the pain is excruciating and does not yield to the usual remedies, a hypodermic injection of morphia should be administered.

In 1908 Nicolaier and Dorn reported that atophan (2–phenylquinolin—4 carboxylic acid) greatly increased the output of uric acid. It is known in the United States under the trade name of cinchophen. Since its introduction atophan has been used extensively in the treatment of gout. The numerous studies made on its effect on blood uric acid and on the excretion of uric acid in the urine have fully substantiated the early claims made for it. As in the normal individual, so in gout, it causes a marked increase in the excretion of uric acid. After its administration, the uric acid in the urine may increase 100 to 200 per cent. in twenty-four hours. Folin and Lyman were the first to observe that the increased output of uric acid is associated with a decrease of the blood uric acid. These observations have been confirmed by McLester, Bass, Fine and Chase and others.

After its discontinuation the uric acid increases rapidly in the blood. Whereas in the normal individual, with continued use of atophan, the increased uric acid elimination lasts only one to two days; in gout this increase continues as long as the drug is given, indicating strongly that the increase is due to the elimination of uric acid stored in the tissues. This would seem to indicate the advisability of continuing its use as long as an increased elimination of acid occurs. Weintraud held that atophan exerts a selective action on the kidneys, particularly on the convoluted tubules, which leads to a freer excretion of uric acid. Folin and Lyman support this renal theory

The usual dosage is 0.5 gm. (7.5 gr.) four times in the twenty-four hours. Some patients possess an idiosyncrasy and suffer from diarrhœa, vomiting, headache and tinnitus. In these cases it should be discontinued and the milder preparation, novatophan (tolysin), administered.

There is convincing evidence that atophan inhibits purin metabolism but this cannot be given here. Experimental work has shown the beneficial effect of atophan depends on the following factors. (1) Stimulation of the kidneys to excrete more uric acid by its selective action on the convoluted tubules; (2) setting free of stored uric acid; (3) inhibition of purin metabolism. In addition to the marked effect atophan has on the excretion of uric acid and on purin metabolism, its influence in relieving pain in the acutely involved joint is often very striking.

Uric Acid Solvents.—Hardly a year passes without one of these much vaunted remedies being introduced to the medical profession. They almost invariably fail to justify the claims made for them. Just as in the case of the alkalis, this is due to these solvents failing to act in a complicated medium like the blood-serum as they do in a test-tube.

Piperazin, lycetol, lysidin, urotropin, urea and urol have all been advocated as uric acid solvents, but all of them have proved failures. Any possible benefit resulting from their use must be attributed more to the fact that patients can be induced to drink more water in this way.

Remedies to Increase the Rapidity of Uric Acid Oxidation.—*Oxygen inhalations* have been tried, but the analyses of Honigmann and Krafft show that there is no diminution of the uric acid excretion, and no evidence to point toward its increased oxidation in the system. Thyroid tablets and spermin have been used for the same purpose, and with the same results. From what is known concerning the action of various enzymes in transforming the various purin bases one into another, and of the action of a special oxidase in destroying uric acid in some of the lower animals, we can only express the hope that some investigator may possibly find that some human tissue does contain an enzyme which destroys uric acid, and that the excess of uric acid in gout is dependent on its absence. Should such a discovery be made, the utilization of such an enzyme might produce results comparable to the action of insulin in diabetes.

Operative Procedures.—Surgical measures are indicated occasionally. When joint tophi become inflamed, and spontaneously open, a persistent discharging sinus may result. In these cases eradication of the tophus is advisable. The bursæ sometimes become inflamed, swollen, and painful, and, in some instances free opening gives great relief. Riedel operated on 2 cases with gouty arthritis limited to one of the great toe-joints. A mistaken diagnosis was made in both instances, the arthritis being thought to be due to a suppurative process. The joint capsule was completely removed without interfering with the bone, and the edges of the incision were brought together without the use of sutures. In both instances the patients lived for years with no recurrence of arthritic attacks, death resulting from other causes. On the basis of these cases, Riedel recommends the ablation of the capsular tissues in those instances in which the arthritis has been confined to a single joint. The removal of the affected joint cannot eradicate the metabolic disturbance causing the disease. Further, we know that patients often go for years without recurrences of the arthritis.

As to the use of *electricity* it may be noted that Remak and Benedikt claim to have obtained good results by the use of the constant current locally applied to the affected joint, both in the acute and chronic form. Labatut, Jourdanet, and Levison, have reported beneficial results by the use of electrical endosmosis, or kataphoresis, with lithion, in the treatment of the joints and skin tophi. The galvanic current, with the electrodes moistened with a concentrated solution of lithion chloride, or carbonate, is passed through the affected joint or tophus, or is given in the form of an electric lithion bath.

Treatment of the Complications.—In cases complicated by *diabetes* the carbohydrates should be restricted. The glycosuria is of a mild type and generally yields readily to dietetic treatment.

Where there are evidences of a serious *nephritis*, the proteins should be partially cut down. If uremic manifestations supervene, as they often do, the usual measures for this complication should be tried.

In the cases with an increasing tendency to *obesity*, the fats and carbohydrates should be cut down, and proteins permitted in larger amounts than would be allowed in the average case.

The *cardiac complications* require special attention. In the cases with evidences of myocardial weakness, the usual cardiac stimulants and tonics are indicated. If the condition be not a too serious one, and the patient's circumstances permit, a course of baths at the Nauheim Springs, in Germany, may help the cardiac features, and will also tend to alleviate the ordinary gouty symptoms. Still, the writer knows of patients with cardiac disease who have actually been injured by this treatment and feels that the greatest caution must be used in advising it.

CHAPTER IV.

OBESITY.

By JAMES M. ANDERS, M.D.

Synonyms.—Lipomatosis Universalis; Adiposity; Corpulency; Fatness.

Definition.—Obesity is a metabolic disorder in which there exists an anomaly of fat metabolism, and characterized anatomically by an excessive amount of adipose tissue; it assumes clinical importance when the fat deposits throughout the body become burdensome or produce impairment of the functions, as shown by disinclination to muscular exercise, palpitation, dyspnœa, and other features. The condition is associated with, and dependent on, a variety of underlying affections; so that it may be rightly regarded as a symptom rather than a pathological entity.

Varieties.—The forms are: (*a*) Simple obesity, which is also termed exogenous obesity; (*b*) endogenous adiposity due to endocrine disturbance. A division of the cases of obesity into general and local should be attempted in practice (*vide infra*).

Etiology. — Predisposing Causes. — *Heredity.*—This was clearly traceable in 330 (or 60.7 per cent.) of 543 cases in the writer's experience, and in some instances, through several generations; it cannot be said to depend upon the indolence of ancestors so much as upon peculiarities of the digestive and assimilative powers. In this group, a history of gout or gout in actual association with obesity was present in 235 (or 43.2 per cent.) of this series of 543 cases. "Rheumatism" was present in 104 (or 35.5 per cent.) of the cases. These figures indicate a close and vital connection between gout ("rheumatism") and obesity.

Hereditary predisposition usually manifests itself early in life, but it may not show itself until a later period or until some exciting cause becomes operative. An inherited tendency is more commonly observed in females than males. Atavism may occur. With Kisch, Oertel, and others, the writer agrees that heredity is not more pronounced in the same sex (*e. g.*, from father to son, and mother to daughter), since his collective investigations tend to disprove this claim.

Age.—In young infants, a marked degree of obesity may occur, and in many cases it is principally ascribable to the milk and farinaceous articles of food in the diet. This form of infantile corpulency is apt to disappear subsequently. Congenital overweight is believed by Englebach and others to be due to cretinism as a rule. Except in girls approaching puberty, obesity in children over six is as a general rule due to an upset endocrine balance, the pituitary gland being commonly at fault. W. Stoye insists that not all cases of adiposity in childhood are due to hypophyseal disease, but some, at least, fall under the head of constitutional adiposity. In the majority of instances, corpulency develops later in life,

in the male between forty and fifty years, and in the female between thirty and fifty years. In advanced years, when retrograde metabolic processes occur, favorable conditions are missing.

Sex.—Obesity, under normal conditions of life, is more common by far in the female than in the male. Personal experience and observations confirm the view that, owing to the lower percentage of hemoglobin in women in comparison with men, the oxidizing energy is correspondingly diminished, and hence a greater tendency to transformation of the carbohydrates into fat. The condition dated from the puerperium in 16.2 per cent. of the writer's series in females, and from miscarriage in 5.3 per cent. In multipara, each subsequent pregnancy increased the general tendency to obesity, in some cases at least. Other factors expressly favorable to the development of an abnormal amount of fat in the female are: The more quiet, inactive life, the greater tendency to indulgence in fat-forming articles of diet, puberty, and the menopause.

Temperament, Occupation, and Enforced Rest.—The indolent, sluggish, luxury- and rest-loving, phlegmatic individual is disposed to corpulency. This fact explains why obesity is so commonly observed among certain races—southern Italians, Orientals, South Pacific Islanders, Dutchmen, and certain African races. A nervous, restless individual expends more energy than a placid inactive person in carrying on a certain definite work and hence is less apt to become obese.

The *occupation* may exert no inconsiderable effect, a sedentary life favoring the development of corpulency. Any calling in which the required muscular activity is at a minimum predisposes to adiposity. The condition often dates from longer or shorter periods of enforced rest—*e. g.*, following accidents and illness. Following such acute infectious diseases as typhoid fever, pneumonia, and the like, adiposity, especially of the anemic form, not uncommonly develops. The writer's notes indicate that out of a total of 543 cases, 43 (or 7.9 per cent.) followed an acute illness.

Exciting Causes.—Simple obesity is especially dependent on the habitual ingestion of abnormally large amounts of fat-making food with or without deficient exercise. The source of the fat is considered to be the fats and carbohydrates taken as food, although probably it is derived to a considerable extent also from the proteins, as seen in the method of treating cases of tuberculosis with milk and raw eggs. Many cases of adiposity are directly caused by disturbances of the internal secretions (*endogenous adiposity*). For example, lack of thyroid function is followed by myxœdema, and von Noorden suggests that a certain number of obese persons, myxœdema apart, owe their fatness to a lessened activity of the thyroid gland. Posterior pituitary hyposecretion produces juvenile adiposity. Following castration there is an increase in the subcutaneous fat deposits, eunuchs being stout as a rule. Again, removal of the ovaries during menstrual life of the female is often followed by obesity due to loss of ovarian secretion and the menstrual flow. Thyroid hyposecretion may supervene and become a factor in causing the obesity. Overeating and underexercise, formerly regarded as the chief etiological factors, are on the whole less potent than endocrine dysfunction, although they may

have an etiological bearing in a considerable percentage of the cases. It is probable that such clinical entities as adiposis dolorosa (Dercum's disease) and Fröhlich's adipositas cerebralis are closely related to endocrine obesity.

Intemperance in the use of *alcohol* plays an important role by inducing hypernutrition. Alcohol is readily oxidized, thus allowing the fat previously present to remain undisturbed. Alcohol also prevents tissue-waste; and finally, certain beverages, as beer, contain starches in considerable amount.

Special Pathology.—The most obvious change is the decided increase in the adipose tissue throughout the body. The fat deposits are most marked in localities in which fatty tissue is normally present, as under the skin, in the panniculus adiposus, and the mammary regions. In cases of adiposity due to endocrine disturbances, the fat deposits have a characteristic distribution to which reference will be made hereafter. The physiological amount of fat has been estimated by Beclard and Quesnay at no more than 5 to 6 per cent. of the whole weight in adults, while the proportion of fat in the new-born varies between 9 and 18 per cent. The normal fluctuations are greater in women (to whom the higher figures also pertain) than in men, and a moderate increase of fat beyond the percentages given above, after the fiftieth year, may be regarded as physiological.

The deposition of fat which always occurs in the connective tissue greatly increases the bulk or dimensions of the body. The round face, "double chin," bulky, deep chest, large waist, conspicuous and sometimes pendulous abdomen, and short, thick, cylindrical limbs, are familiar. It is to be observed that corpulency, "fatty infiltration," and "fatty degeneration," are not synonymous terms.

The various viscera, more particularly the *heart*, are overlaid with fat, and the interstitial connective tissue may be the seat of fatty infiltration. Out of 103 cases, lasting for periods ranging from a few to many years, of extreme adiposity that have occurred in the writer's experience, 5 cases gave clinical proof of the existence of true fatty infiltration. This morbid process (infiltration) is limited to a thin layer of the intermuscular fibrous tissue, situated directly beneath the epicardium, and is not to be confounded with true fatty infiltration.

Hypertrophic dilatation of the heart is frequently present in high degrees of plethoric adiposity, owing to an enlarged volume of blood, and the arteries may show fatty changes in the intima and media, and later those of arteriosclerosis. The *veins* are often the seat of larger or smaller varicosities. The *kidneys* and *lungs* may be enlarged owing to fat deposits and fatty infiltration. Additionally, passive congestion and œdema of the lungs, secondary to the cardiac weakness, may be found at autopsy. Of the viscera, the *liver* alone is the seat of normal fat deposits, but in obesity these accumulations may cause enlargement of the organ. The *stomach* may be dilated.

Pathogenesis.—Fats conserve the albumin in metabolism by furnishing heat and force during their combustion—an important chemico-physiological function. The origin or mode of formation of the excessive fat accumulations is a subject that is imperfectly understood. The energy

derived from food is reckoned by calories of heat produced during the combustion of the latter. It is clear that when the energy taken in food exceeds the energy expended in work, heat and exercises, an accumulation of fat is the result. It makes slight difference whether the calories are supplied in the form of fat, carbohydrate or protein. Strouse, Wang and Dye,[1] Means[2] and others have shown that there is no characteristic change in the basal metabolism of the obese, although they found that obesity in certain persons may occur on food intakes much below their calculated caloric requirements; furthermore, the specific dynamic action of protein is decidedly less marked in the obese than in the normal. It seems probable, however, that this applies to the excessively obese to those who exemplify the dystrophies—rather than to moderately fat persons (McLester). Arnoldi[3] emphasizes the differences in the metabolism according as the vagus or the sympathetic system predominates abnormally. In the anemic variety a deficiency in oxidizing power may be assumed to exist and constitute a causative factor. Under these circumstances, a normal proportion of carbohydrates in the aliment used will fail to be destroyed on account of deficient oxidation. Obesity, therefore, may be said to be dependent on disturbance of cell-activity. The disturbance of the metabolic processes may be transmitted through heredity.

Histology. Microscopically, differences in the size and number of the fat globules are exhibited. Thus, in the plethoric form of obesity the fat globules are large, being distended with droplets of fat; their cell envelope and nuclei, however, are quite indistinct. When numerous, the fat vesicles are closely packed and their surfaces are faceted by mutual pressure. In cases in which anemia is associated, the fat masses are soft and doughy to the feel, the cells are less completely filled, and the cell membrane and nucleus are easily distinguishable.

The process of fatty infiltration begins with the appearance of a small droplet within the cell envelope; this grows larger until "the cytoplasm forms a mere capsule about it and the nucleus is crowded and flattened in consequence." Microscopic sections, stained in the usual manner, do not show the presence of fat globules, but in the spaces previously occupied by them vacuoles are seen.

Symptoms.—At first, slight inconvenience, a sense of burdensomeness, and dyspnœa during walking or working, are the principal subjective manifestations, and, indeed, no other symptoms may be complained of for years. Later, with the slow and gradual development of the disease, and involvement of the various viscera, both the number and intensity of the clinical features are increased. Marked breathlessness on exertion, due to the hampering of the action of the heart and lungs by massive chest walls, fat overgrowth and the upward crowded diaphragm, are among the earliest conspicuous features. The blood-pressure is somewhat above the normal in most cases of obesity. Aubertin,[4] however, rejects

[1] Studies on the Metabolism of Obesity; Preliminary Report, *Jour. Am. Med. Assn.*, 1924, **82**, 2111.

[2] Studies of the Basal Metabolism in Obesity, etc., *Jour. Med. Research.*, 1915, **27**, 121.

[3] *Ztschr. f. klin. Med.*, June 30, 1922, p. 94.

[4] *Jour. Am. Med. Assn.*, 1922, **79**, 1367.

the assumption that adiposity can cause high blood-pressure, but its coincidence with morbid conditions in which high blood-pressure is common is to be remembered. Brown and Keith[1] conclude that the circulating blood and plasma volume, when compared to body weight, are smaller in obese than in normal persons. With reduction in weight, they found that a decrease or increase of circulating blood volume may occur. The married female is often sterile, if excessively obese. The symptoms presented by individual patients will vary according to the stage at which they come under observation.

In the *plethoric* form there is hypernutrition of all the tissues. In addition to the excess of fat, which is symmetrically distributed throughout the body, as a rule, the muscles, including those of the myocardium, are vigorous and voluminous. The blood shows a condition of abnormal richness both in erythrocytes and hemoglobin. In a number of patients the erythrocytes are over 6,000,000 and the hemoglobin over 110 per cent. The blood shows an increase in specific gravity, fluctuating, however, between 1.062 and 1.070, and that of the serum between 1.032 and 1.035. Von Noorden states that the erythrocytes and hemoglobin are normal in the plethoric forms as a rule, although rarely polycythemia is observed.

The so-called *anemic* form, of less common occurrence than the preceding, occurring usually in women, is characterized by and probably dependent on anemia. Muscular exercise is difficult and early induces exhaustion, accompanied by distress of breathing and cardiac palpitation. The *symptoms* are in a measure those characterizing the anemias in general, together with a peculiarly marked increase of fatty depositions in the usual places of predilection. The writer has the records of blood examinations in 19 cases. In the majority of the instances the blood changes were of the chlorotic type. The hemoglobin percentage varied greatly—from 33 to 83 per cent.—the average being about 70 per cent. In about 35 per cent. of the cases, however, the erythrocytes and hemoglobin were reduced about equally. More or less poikilocytosis was commonly found; and also an occasional normoblast and a considerable leukocytosis (the count ranging from 11,000 to 31,000 per cmm.) was present in about 25 per cent. of the cases. Brugsch,[2] however, claims that in the anemic forms the red cells are often above the normal with a decrease, or no relative increase, in the percentage of hemoglobin.

Physical Signs.—The complexion is often florid, the skin soft, smooth and in some cases the face looks congested; the lips, conjunctivæ, and other mucous membranes present a rosy hue. The neck is massive, the abdomen prominent, and the girth decidedly increased. The sweat glands are unusually active. But though the heart systole is abnormally strong, the impulse is felt indistinctly on account of fatty overgrowth and the subcutaneous fat. Later, as the result of myocardial weakness, and often before this in extreme cases, the impulse may be lost, both to inspection and palpation. The pulse is slow as a rule.

Indications of cardiac enlargement are present. In well-marked cor-

[1] *Arch. Int. Med.* 1924, **33**, 217.
[2] Fettsucht. In *Kraus-Brugsch Handbuch*, Bd 1, 1922.

pulency, however, it is always difficult, and sometimes impossible, to establish the boundary lines of dulness by percussion. The heart sounds remain clear for a long period, but with the progressive development of the condition become indistinct. Murmurs may be audible, most commonly in the aortic zone; they are probably not due to chronic valvulitis, but to either a roughened condition of the intima of the aorta or to relative incompetency. In cases with associated anemia inspection shows pallor of the bodily surface and the visible mucous membranes. The skin is inclined to free perspiration, and, in advanced cases may become wrinkled. "The skin is often irritated (intertrigo) by the excessive sweating and by friction of cutaneous surfaces in the folds of fat, as under the breast, at the abdominal and inguinal folds, and around the scrotum and labia. This may be followed by eczema." To the feel, the subcutaneous fat-cushions are soft and flabby and the muscles are lacking in firmness and strength. The signs of cardiac insufficiency become more or less conspicuous with the progress of the condition, and at last, as the result of falling arterial pressure, dropsy supervenes. Characteristic hemic murmurs are often heard. In some instances the menses may be both scanty and irregular, and dysmenorrhœa may form the burden of complaint.

The appetite is impaired and capricious; in most cases carbohydrates are preferred to proteins. The tongue is furred and the breath often foul. Intestinal flatulence with more or less constipation is the general rule. The daily quantity of urine voided is small, due to diminished arterial pressure. Slight albuminuria is often found and is to be ascribed to passive congestion in the majority of instances, since, with improved circulation as the result of the use of cardiac stimulants, the albumin usually disappears.

The subject of obesity does not resist well the acute infections, and his fat-laden viscera are likely to show degenerative changes at a premature period of life.

In another group, the condition, if unchecked, leads to a marked increase of the general bulk of the body and various grotesque malformations. The features are broad and coarse, and some of the facial lineaments are obliterated. The maximum weight among the writer's patients was 412 pounds, and Weinberger observed a boy, aged ten years, weighing 266 pounds. At last locomotion may be impossible.

In some cases the muscular power diminishes rapidly, the appetite fails, profuse sweatings occur, and signs of general venous stasis may be observed. In the majority, however, venous engorgement develops more insidiously. Cough, distress of respiration, and asthmatic seizures, especially at night, signal the passive hyperemia of the respiratory mucous membrane. The symptoms of a gastric catarrh, dependent on stasis in the mucous membrane of the stomach, are in evidence, and with these the characteristic features of gastrectasis may be combined. From analogous changes in the intestines, there is often constipation which may alternate occasionally with diarrhœa. The passive congestion of the kidneys is shown by a tendency to oliguria with albuminuria, and the presence of hyaline and a few granular casts.

The products of tissue-metabolism are not eliminated in the normal ratio. Indeed, the writer has found that the daily renal output may be diminished one-half while the amount of food ingested is plus. Sexual desire is in abeyance and azoöspermia is not uncommon.

In the last stage of the plethoric form of obesity, malleolar œdema merging into progressive dropsy may arise and lead to a fatal end. Death may also come suddenly from cardiac paralysis.

Endocrine Disturbance.—In *pituitary adiposity*, the chief deposits are usually confined to the epigastrium or lower abdominal regions and to the thighs. The shoulder girdle is also, although less prominently, affected except in the most marked cases when the deltoid region shows considerable padding. Again, the lateral aspects of the lower portion of the thorax show deposits of considerable size. It begins, as a rule, in the juvenile age or between the sixth and fourteenth years, although posterior pituitary obesity may also be met with in adult life. In myxœdema or thyroid hypofunction, the fat pads are evenly distributed, including the dorsal hands and supraclavicular regions. The skin and mucous membranes, including the tongue, are thickened by myxœdematous infiltration and the face presents a mask-like appearance, the usual lines of expression being obliterated. The voice is leathery, the speech thickened and slow, and articulation difficult. The mental processes are likewise sluggish.

In true *gonad adiposity* which usually occurs after the thirty-fifth year of life, there is a disproportionate mammary enlargement as compared with the adiposity in other parts of the body, and also "an apron of mons veneris shelving and decided localized trochanter padding, with a diffuse, even fulness of the upper thighs, extending to the knees" (Engelbach). It is to be recollected that two or more glandular disturbances may be present in a single individual (pluri-glandular adiposity). Most instances of endocrine obesity begin as uniglandular deficiencies, while later other glands show involvement; for example, pituitary and thyroid hypofunction are commonly combined in the same individual and less frequently also gonad dysfunction. In such instances, the clinical symptoms and course of each uniglandular disturbance must be duly appreciated as the result of a close analysis.

Complications and Sequelæ.—Among the principal complications, often the precursors of the terminal stage, are bronchitis, pulmonary congestion, anginal attacks, dyspnœa, hernia, albuminuria, diabetes mellitus, arteriosclerosis, especially of the aortic arch and the coronary arteries, œdema, cerebral hemorrhage, and Cheyne-Stokes respiration. The dyspnœa, which is sometimes troublesome, is dependent on pulmonary congestion as the result of "light" breathing and feeble heart action during sleep. Severe attacks of angina are also observed. Preble,[1] who made observations on 1000 cases, found that 432 showed evidence of organic, and 230 of functional heart disease. His observations also showed evidence of kidney impairment in 463 of the 1000 cases, while chronic nephritis was diagnosed in 53 cases, and albuminuria without nephritis in 410. Diabetes is from ten to twenty times more common among the fat,

[1] *Boston Med. and Surg. Jour.*, April 23, 1923, p. 613.

and two and a half times more common among the Jews (Joslin[1]). Paulin and Sauls[2] found that of 26 cases of obesity 15 or 57.6 per cent. gave an abnormal response to the ingestion of glucose. Fatty infiltration may occur as a sequel, but it is extremely rare.

Circumscribed Obesity.—In many cases the fat depositions are not distributed regularly over the entire body, but are confined to circumscribed portions—for example, the abdominal parieties, the mammary regions, and the hips. Williams[3] points out that localized superfluous fat-deposits are due to lack of exercise of the underlying muscles, and attributes the "abdominal figure" to insufficient exercise of the muscles of the abdomen.

Diagnosis.—This is not difficult in well-marked instances. Care must be exercised in detecting associated conditions, as gout, anasarca, arteriosclerosis, and the like; also the complications and sequelæ. In the early recognition of a *gland deficiency*, the age of the patient and the distribution of fat deposits are most useful aids. It may be assumed that the longer the duration of cases of endocrine dysfunction, the greater the likelihood of secondary glandular participation. That special form of fat deposit known as *adiposis dolorosa* (Dercum's Disease) is characterized by nodular and diffuse pads usually about the arms and trunk and less commonly about the legs; by pains and tenderness over the affected areas and marked asthenia and psychic disturbances. Other clinical features not seen in ordinary obesity, are hemorrhages from the mucous outlets, parasthesias, ecchymoses from slight injuries and pigmentation of the skin.

In *dystrophia adiposo-genitalis* (Fröhlich's syndrome), general adiposity is accompanied by infantilism and mental and physical lethargy. The principal cause is a hypophyseal tumor which depresses pituitary and possibly other glandular functions.

Prognosis.—This depends principally upon the degree, variety, and prevailing complications of each individual case. In the earlier stages in cases in which the ingestion of too much fat-making food is the principal cause, the outlook is positively favorable under appropriate treatment. In more advanced cases, with associated arteriosclerosis, particularly of the coronaries, stenocardia, and œdema, the prognosis may be of the utmost gravity. Adiposity caused by thyroid dysfunction usually responds to thyroid medication at any stage, if we except the congenital form (cretinism), but overfatness due to posterior pituitary and gonad deficiency gives a far less favorable prognosis under specific treatment unless instituted quite early. Medical officers of life insurance companies recognize obesity as an indication of impaired health, and when the body weight is decidedly disproportionate to the height of the individual, the risk is usually declined. Moses[4] concludes from his statistical investigation into the subject, that the duration of life among adipose persons is two and a quarter years shorter than among the non-corpulent. In

[1] *Jour. Am. Med. Assn.*, 1924, **83**, 727.
[2] *South. Med. Jour.*, vol. **15**, p. 2511.
[3] "Some Aspects of Obesity," *Practitioner*, May, 1904.
[4] *Reichs-Medizinal Anzeiger*, 1920, **45**, 83.

obesity due to alcohol, the outlook is especially unfavorable. When physical exertion induces early breathlessness, thoracic oppression, and palpitation, and the pulse becomes small and irregular, the outlook is gloomy. Joslin states that diabetes mellitus is from ten to twenty times as frequent among obese persons as among those of normal weight. The statistical studies of Anders and Jameson also indicate that adiposity has a potent predisposing influence in diabetes mellitus.

Modes of Death.—Among the commoner causes of death are: Angina pectoris, apoplexy, syncope, uremia, cardiac dilatation, intercurrent acute infections, and necessary major operations. Of the rarer modes of death may be mentioned rupture of the heart, cerebral thrombosis, hemorrhagic infarctions, carbuncles (to which subjects of obesity are liable), and pulmonary œdema.

Treatment.—Prophylaxis.—A child of a mother suffering from anemic obesity should be nourished by a suitable wet-nurse who is not predisposed by heredity to this form of obesity. In the earlier years of persons showing a hereditary disposition to corpulence, unless clearly due to hypofunction of endocrine glands, the fat-forming (farinaceous) substances must be greatly restricted in the dietary. Physical exercise should be advised and encouraged. Cool bathing is a useful prophylactic measure if carried on systematically and regularly. If anemia is associated during childhood, suitable forms of iron should be administered. At middle life, in those disposed to corpulency, all imprudences in eating and drinking should be avoided. Outdoor sports and gymnastics should be used carefully. Prophylactic measures, however, must have reference to the special indications presented by individual cases. Again, the special etiological factor may be a definite endocrine disturbance which demands early specific medication.

The treatment of confirmed obesity may be conveniently discussed under three heads: (*a*) The dietetic treatment; (*b*) the mechanical management (to increase oxidation or heat production); (*c*) the medicinal measures. There are few diseases that the physician is called upon to treat in which it is so vitally important to adapt the treatment to the patient as in obesity. If the dominating etiological influence is removable, this should be accomplished in the first instance. Patients who present complications of various kinds require very careful oversight. Finally, that method must be selected which invigorates rather than weakens the patient.

Dietetic Treatment.—Despite the accepted fact that endocrine dysfunction is a principal cause of adiposity, the dietetic management of a considerable percentage of the cases which cannot be traced to endocrine disturbances is still quite important. Broadly speaking, the principal variation from the ordinary dietary consists in a restriction of the fat-forming food, or carbohydrates. The carbohydrates should not be totally withdrawn, since the ingestion of large amounts of protein foods may excite digestive disturbances, gouty manifestations, and even chronic interstitial nephritis. It is the writer's almost invariable custom to allow a limited proportion both of carbohydrates and fat, and thus accomplish two objects: (1) A slow consumption of the previous fat depositions;

(2) maintenance of the normal metabolic processes, or at all events only slight disturbance of the nitrogen balance.

The principal systems of *dietary* are known by the names of Banting, Ebstein, and Oertel. In so-called "Bantingism," sugars, fats, and starches are greatly restricted in the dietary; water, however, is not reduced, and wines and spirituous liquors are allowed. Sir Dyce Duckworth well said that as a system "Bantingism" is both unphysiological and impractical. In subjects with a gouty diathesis Banting's heavy protein and alcohol dietary is contraindicated.

In Ebstein's diet-list the proteins are diminished, and carbohydrates greatly restricted, while fat is freely permitted. It is assumed that fat does not increase stored fat, and being less readily oxidized than the carbohydrates, it interferes less with the protein metabolism. Saccharine matter and potatoes are strictly forbidden.

The Oertel method is especially adapted for some cases of obesity with feeble hearts. This author allows more fat than Banting, but less fat and more (about double the quantity) proteins and carbohydrates than Ebstein. The amount of *free* water permitted daily is only one pint; about one pint additional in food is allowable. His diet-table for obesity is appended:

	Albumin.	Fat.	Carbohydrates.	Calories.
Minimum	156	25	75	1180
Maximum	170	45	120	1608

Oertel also offers a special diet list in circulatory disturbances which comprises three parts:

1. The reduction of the amount of liquid taken with meals and during the intervals, the total for each day being 36 ounces (1064 cc.). Frequent bathing (including the Turkish bath in suitable instances) and pilocarpine are employed to promote free diaphoresis.

2. The diet is composed largely of proteins, as follows:

Morning.—A cup of coffee or tea, with a little milk—about 6 ounces (180 cc.) altogether; bread, 3 ounces (90 gm.)

Noon.—Three to 4 ounces (90 cc. to 120 cc.) of soup; 7 to 8 ounces (218 gm. to 248 gm.) of roast beef, veal, game, or poultry; salad or a light vegetable; a little fish; 1 ounce (32 gm.) of bread or farinaceous pudding; 3 to 6 ounces (90 gm. to 180 gm.) of fruit for dessert. No liquids at this meal, as a rule; but in hot weather 6 ounces (180 cc.) of light wine may be taken.

Afternoon.—Six ounces (180 cc.) of coffee or tea, with as much water. An ounce of bread as an indulgence.

Evening.—One or two soft-boiled eggs, 1 ounce (32 gm.) of bread, perhaps a small slice of cheese, a little salad, and fruit; 6 to 8 ounces (180 cc. to 240 cc.) of wine, with 4 or 5 ounces (120 cc. to 150 cc.) of water.

3. Graduated *exercise*, as walking, the distance to be undertaken each day to be carefully specified and frequently, though gradually, increased. A like plan is to be pursued with reference to the degree of inclination. This stregthens the heart muscle. The Oertel method has gained an enviable reputation in Europe where special sanatoriums for its administration have been established. At these "Terrain curorte" are to be found, "health paths" of four different grades, differing in slopes from 5 to 20 degrees. The majority of these paths are provided with sign-boards giving distances and elevations.

A. W. Perry pointed out that there are cases in which an excessive amount of water (serum) in the tissues is practically the sole cause of the corpulency. He recommends Ranke's normal diet; namely, meat, 280 gm.; fat, 100 gm.; bread, 400 gm.; and the limitation of the amount of fluid ingested, allowing only 300 to 400 cc. more of water to be taken daily in drink and food than the daily amount of urine secreted. In order to carry out this method the percentages of water in different forms of food prepared ready to be eaten must be carefully estimated. These are "(numbers indicate percentages of water): Soup, 91.6; boiled meat, 70; roast mutton, 74; roast beef, 59; roast veal, 78; dried meat, 40; fish, white, 74; pudding, 48; mushes, 80; bread, hard, 30; bread, soft 40; carrots, boiled, 82; spinach, 83; peas, 69.5; lettuce, 97; fresh fruits, 85; string beans, 88; celery, 84; asparagus, 94; milk, 87; cream, 65; cheese, 35; baker's toast, 1.18; crackers, 7.50; potatoes, boiled, 70."

Under any system of dietetic treatment the patient should be weighed accurately at brief intervals. The food should also be weighed and measured at first, but the patient soon learns to estimate by bulk the requisite quantity of each article permitted. The effect of treatment upon the general health must be noted. Fat-reduction must always be *slowly* progressive. If the case is one of plethoric obesity, a judicious rearrangement of the food, *e. g.*, a moderate increase of the protein substances and a coresponding diminution of the carbohydrates, is indicated. The majority belong to this type, and the writer is in the habit of ordering the following dietary, with modifications to suit individual cases:

Morning Meal.—Fruit—as an orange, or one-half a grape-fruit (without sugar), or a sour apple, wheat bread, 1¼ ounces (gm. 40); a soft-boiled egg; milk, 1 ounce (28 cc.); coffee, 4¼ ounces (120 cc.).

Noon Meal or Luncheon.—Caviare, 2 drams (gm. 8); lamb chops, boiled ham (cold), or fowl or game in season, 2 to 3 ounces (gms. 60 to 90); salad, 1 ounce (gm. 30) (with a small amount of French dressing); cheese, 1 dram (gm. 4); bread, rye, or bran, ½ ounce (gm. 15); fruit (except strawberries and bananas), or (instead of the latter), water, 4 ounces (125 cc.).

Evening Meal or Dinner.—Soup (clear), 3 ounces (85 cc.); fish, 2 ounces (gm. 60); roast or broiled beef, lamb, veal, or game or poultry, 3 to 4 ounces (gm. 94 to 112.5); one or two of the following green vegetables: spinach, string beans, green peas, celery (stewed), asparagus, raw sliced tomatoes, Brussels sprouts, 1¾ ounces (gm. 42). For *dessert*, may take plain rice pudding, junket, cup custards (all sweetened with saccharin) or fruit (except strawberries and bananas) either raw or cooked, 4 to 5 ounces (gm. 125 to 150). May take 4 to 5 ounces (125 to 140 cc.) of water when fruit is not used.

No fruit is to be taken at meals except as indicated above, but a glass of water on rising, and three hours after food, is permitted. During the warm season, particularly if the sweat glands are active, an additional glass of water may be occasionally allowed.

In cases of anemic obesity, the restriction of fluids may be more rigidly enforced. The rule, in such instances, is to favor concentration of the blood by not allowing more than 32 ounces of fluid *per diem*. In any given instance in which increasing weakness of the heart, with an impeded circulation, naturally diminishes the excretion of water by the cutaneous and renal routes, the consumption of fluid must be limited. The value of highly nutritious blood-making food—tender meats, milk, eggs, green vegetables, fruits—in this form of obesity is undoubted, and indicated first of all. The great difficulty in these cases is to secure sufficient muscular exercise, such subjects being lethargic and strongly averse to physical

exertion. The writer agrees with Osler that "in the treatment of extreme obesity the patient should be in a hospital or under the care of a nurse, who will undertake the proper weighing and administration of the food."

The Mechanical Treatment.—The special form of exercise, and also the duration and frequency, must be carefully adjudged for the individual patient. At the commencement of treatment in well-marked cases and when circulatory disturbances are manifested, it is advisable for the patient to take little exercise, and in extreme cases, he should have absolute rest, until the fat deposits have, in a measure at least, been removed. One of the principal uses of exercise is to maintain an appropriate proportion of albumin in the body, but "not only the fat but organic albumin is likewise used up by muscular activity" (Oertel). Physical exercise promotes the destruction of the fat already warehoused in the system, and, moreover, it aids cardiac action and induces deeper breathing. The writer's best results have been from walking out of doors, later by increasing the pace, and, finally, climbing exercises either at home or at open-air health resorts, combined with gymnastics for the arms and trunk. Golfers and tennis players may be encouraged to pursue their favorite games in a systematic manner, but with moderation, if there be no contraindications due to associated conditions or cardiac insufficiency.

It is all-important to make the minutest study of the patient's cardiovascular system, and to observe the effect of the muscular exercise. In the anemic form, the patient begins with short walks on the level, to be slowly and gradually increased as the force of the heart and strength of the patient permit. On the other hand, in the plethoric form, a greater amount of physical exercise and even walks up inclines of moderate degree may be taken from the commencement. The so-called "resistance exercises," introduced by the Schotts in the treatment of chronic cardiac diseases, may be employed when cardiac dilatation is associated. Great care must be exercised in prescribing mechanical treatment in obese patients who have atheromatous vessels. Complications must be relieved by appropriate treatment. When oxidation cannot be sufficiently promoted by muscular exercise, a course of rather deep massage, with Swedish movements, is the best substitute.

Although to a lesser extent than the muscular exercise, *balneotherapy* also promotes oxidation. When no contraindications exist, cold- or salt-water baths followed by active hand-rubbing by the patient may be advised. These baths should be brief and the temperature of the water not too low at the start. Kisch[1] recommends carbon dioxide baths in cases of obesity in which gaseous distention of the abdomen or arteriosclerosis is present; he also advises warm baths in cases of endocrine origin. If gouty manifestations are prominent, hot baths are to be employed preferably, since they increase elimination through the skin.

The treatment of associated diseases, many of which stand in the relation of cause is highly important—more especially gout. It is decidedly inadvisable to institute the usual reduction treatment when gout and obesity are combined, since such a course aggravates the first-named

[1] *Die Balner therapie der Fettsucht Therap. Halbmonatshefte*, 1921, vol. 35.

disease. The most brilliant results in such cases are obtained by adapting the treatment principally to the gouty element.

Medicinal Treatment.—A number of watering-places, particularly Marienbad and Carlsbad, enjoy an enviable reputation for the treatment of obesity. They are better suited to the plethoric than to the anemic form of obesity, or those presenting serious cardiovascular disease (Hinsdale). It is obvious that cases of adiposity due to endocrine disturbances would not be benefited by a sojourn at these resorts. Such a course of treatment is not to be pursued except under the strict supervision of a resident practitioner. The results obtained are rarely permanent. In mild grades of plethoric obesity, such places as Kissingen, Brides-les-Bains, and Vichy, abroad, and Saratoga and Virginia Hot Springs, at home, may be recommended. Kisch, however, lauds Glauber salts springs in cases in which arteriosclerosis is associated in comparatively young subjects.

Certain remedies recommended for obesity are harmful—*e. g.*, phytolacca berry. The use of thyroid gland preparations has come into favor. In the treatment of myxœdema, thyroid preparations yield satisfactory results. The commencing dose of thyroid extract should not exceed $\frac{1}{2}$ gr. (0.03 gm.) thrice daily, to be increased at the end of one week to a grain (0.065 gm.) with the same frequency. The dosage may be carried to 2 gr. three times a day, if it be found necessary to obtain the result desired; but amounts beyond this are rarely advisable. In congenital hypothyroidism (cretinism) "before the age of six months, $\frac{1}{50}$ gr. (0.0013 gm.) of desiccated thyroid substance once a day is given, and gradually increased by $\frac{1}{50}$ gr. until the toxic effect, or until the relief of signs and symptoms, is produced" (Engelbach). An increased rectal temperature or a sudden great loss of weight (one or both) is a signal of toxic effects, and the remedy should be temporarily withdrawn. In the adult, thyroid intoxication is shown by restlessness and an increase in the pulse-rate to 100 or over, and is an indication for stopping the remedy for a few days when it may be resumed, but in doses smaller than those that produced the intoxication. After the myxœdematous pads and the dryness of the skin have disappeared, the intermittent use of the thyroid preparation must be continued indefinitely. It has been my custom to administer the desiccated thyroid extract during every third week and this has usually sufficed. In some instances, however, it has been found necessary to give it during alternate weeks.

Some observers have reported good results from the use of thyroid extract in the anemic, flabby, "myxœdematoid" form of obesity. In a number of cases belonging to this category the use of thyroid extract (desiccated) in small doses caused a progressive loss of weight without injury to the general health in my experience. Granting that the thyroid hormone is a general cell stimulant, in the majority of these cases, however, the loss is not maintained after a reduction of 10 to 15 pounds. It is wise to guard the heart by combining small doses of digitalis. Pituitary and suprarenal extracts seem to increase the efficacy of the thyroid treatment in children (Lereboullet). Single products, however, should be employed rather than pluriglandular preparations at the onset.

In the treatment of *juvenile obesity* due to hyposecretion of the posterior lobe of the hypophysis, one may employ pituitrin hypodermatically, or the extract of the entire gland by mouth. The latter should be given in doses of 10 to 20 gr. (0.6 to 1.4 gm.) after meals. Of pituitrin, the commencing dosage is 5 minims (0.3 cc.), increased by 1 minim (0.06 cc.) each day until the patient experiences a cramp-like or colicky sensation in the abdomen, attended with a bowel evacuation ("intestinal reaction"). This remedy may also be given by mouth, the commencing dosage being 15 to 20 minims (1 to 1.3 cc.) a day and increased 2 to 3 minims (0.12 to 0.18 cc.) each day until the characteristic reaction mentioned above is obtained. In infants and children 1 minim (0.06 cc.), or if under one year of age, a fraction of a minim, is used as the initial dose (Engelbach). The effect of this special medication must be carefully noted by weighing the patient at intervals and making careful circumference measurements. Finally, it is to be recollected that not all patients respond favorably to a course of intensive treatment by the pituitary extracts.

The treatment of obesity due to *gonad insufficiency* by various ovarian substances has not been satisfactory in the past. It is probable, however, that these substances have not been given in sufficiently large doses. It is advisable to employ the substance of the entire gland, giving 10 to 20 gr. (0.65 to 1.3 gm.) four times daily. Engelbach states that ovarian substance of the whole gland should also be administered hypodermically in doses of 1 to 5 or 6 cc. daily. In many cases of recognized endocrine obesity, the physician must depend largely upon dietetic and hygienic measures to bring about the desired reduction of weight. Indeed, success in the treatment of obesity depends almost wholly upon careful attention to the details of administration of glandular products, and also, to its hygienic and dietetic management.

The cathartic mineral waters are indicated in cases in which there has been gormandizing with disturbance of the portal system, and in cases of plethoric obesity. When saline laxatives are employed the other fluids must be correspondingly reduced. The state of the heart and bloodvessels must always be considered. In obese subjects, surgical risks are greatly increased (Kirschner). Appropriate treatment before operation, however, simplifies the surgical problems in connection with adiposity.

Treatment of Local Obesity.—The best method is a course of local massage combined with a mild general-reduction cure. Allard[1] recommends the employment of a vibrating ball controlled by an electric motor in circumscribed obesity; this method of treatment has proved efficient in a limited number of cases. When the abdomen is the seat of the localized overfatness it is well to estimate the elements of intestinal distention, and gastrectasis when present and to institute appropriate measures, such as massage.

[1] *Revue de therapeutic*, 1905, No. 6, p. 191.

PART II

DISEASES OF THE DIGESTIVE SYSTEM

CHAPTER V

INTRODUCTORY DISCUSSION ON THE DISEASES OF THE DIGESTIVE APPARATUS

By CHARLES G. STOCKTON, M.D.

In the primitive unicellular forms of life the chief concerns are with the absorption of nutriment and the discharge of waste, that maturity may be reached and cell division occur. When cells are assembled into complex organisms, with systems, apparatuses and organs having coördinating functions and common purposes of existence, there still remain predominant those primary needs of nutrition essential to organic life. As digestion is a preliminary but necessary step in nutrition, the diseases of digestion are seen to possess fundamental and far-reaching importance. There is a biological inferiority in certain strains expressed in feeble nutrition, sometimes rooted in definite embryological defects in the digestive tract, in other instances in functional weakness the cause of which is not evident.

1. **The Whole and the Part.**—We are accustomed to look upon digestion as the function of an extensive and complicated apparatus, but it is so intimately related with the functions of other parts of the body that it is difficult to draw lines of precise limitation beyond which it can be said digestion has no part and receives no reciprocal activity. We commonly speak of the digestive apparatus as including the alimentary tract and those important glands which contribute specific secretions to the advancement of digestion; but as absorption and assimilation, on the one hand, and the formation and withdrawal of katabolic and waste products, on the other, are immediately related to the preliminary digestion, it is impossible to form a clear conception of the diseases of the digestive organs without taking into consideration the state of other and contributing parts of the organism. While it makes for simplicity in description to exclude from implication those organs not commonly grouped with the digestive apparatus, this does not result in a correct understanding, and, therefore, if one is to find an explanation not only for a disturbed physiological state, but also, in instances, for structural changes in the digestive organs, he must widen the field and direct his study to the nervous system including its psychical manifestations, to the fluids of the body, to the general and the portal circulation; the metab-

olism and the elimination. The importance of these matters is perhaps unconsciously recognized when we declare that good digestion depends upon restful sleep, fresh air, sunlight, physical exercise, and the proper activity of the bowels, kidneys, and skin. When we disregard these essential matters, it is difficult to form a just conception of the nature of digestive disturbances, or to prescribe successfully therapeutic measures for their relief. For this reason one may truly say of a given dyspeptic, the trouble arises in the brain, or in the lungs, the heart, the kidneys, etc. The pathology of stomach diseases is not limited to that organ, but is the expression there of disturbances that may be widely distributed through the whole body. This fact applies to other parts as well as to the stomach. Answering Virchow's question. "Where is the disease?" we have sought to give each disease a local habitation, but this is only a relatively justifiable conception as regards any disease, being more true of some than others. There are probably no diseases referable solely to the kidneys, the heart, or the blood; the man is sick, and it appears here or there.

Although a large proportion of the affections of the digestive apparatus are functional, many cases with which we are confronted present an association of functional and structural abnormalities. Congenital malformations, displacements of abdominal viscera, and hernia, both internal and external, are structural defects; the infiltrations like amyloid disease, the more specific infections like cholera, typhoid fever, amœbic dysentery, and tuberculosis must be regarded as beginning their effects upon the body through their action upon its structure. But almost immediately these lead to functional disturbance, both local and general, and therefore the state of general vitality of the patient conditions the functional activity of each organ, and is a potent factor in the outcome of any local disease.

Many facts relating to digestion have come into our possession during the past twenty years, but the mere knowledge of facts or their presentation in isolation is not the most satisfactory method of studying a subject. By what laws are these facts related? In what is the favorable activity of one organ dependent upon that of another? Of the various links in the digestive chain, which are the more indispensable? If we shunt the action of certain parts through surgical intervention, what will be the final result in the organism? These are questions of vital importance, and by arranging our data with a view to answering such inquiries we throw most light upon the subject as a whole.

2. **Individuality in Disease.**—It is necessary to value carefully the individual equation. On the one hand misconception may arise when generalizations are based on the manifestations of a single case. On the other hand the question of individual peculiarity and idiosyncrasy must be carefully weighed, so that we may avoid the feudality of classification and the tyranny of established rule. Anthropology shows that there is a predisposition to certain disease in individuals of a special type, as in those having congenital defects affecting the structure and function of glands of internal secretion. Draper holds that there is a typical conformation in the rheumatic, the tuberculous and in those who suffer from

nutritive defects. Even in peptic ulcer, a special physique may be recognized and Fleiner long ago pointed out the weaknesses that accompany ptosis of the internal viscera. Thus infections may more readily find lodgment in types that provide the suitable anthropologic background. Through idiosyncrasy, foods, although usually acceptable in an occasional individual invariably excite intense gastro-intestinal distress. This action is explained probably by anaphylaxis. We must not forget that anaphylaxis itself may depend upon a disturbance of internal chemistry having its origin in infection. Idiosyncrasy applies to other matters than food. The sensitiveness of some persons to the ill effects of mental excitement, physical fatigue, or exposure to cold must not be overlooked, nor must it be cast into a rule.

3. **The Interrelation of Digestive Functions.**—Common experience has taught us that the mental state and the sense of taste in some unknown way affect the primary digestion. Thus worry induces leanness, and happiness favors the opposite condition, in a measure independently of the amount of food taken. Some of the steps by means of which these effects are obtained are explained by the work of Pawlow. The digestive secretions and the motor activity of the stomach and intestine are excited by proper psychical stimulation. Distress may either inhibit or overexcite. Hirsch and von Mering have established the fact of an intimate relationship between gastric secretion and motion, and the secretions of the duodenum, pancreas, and liver. The presence of acid gastric juice in the duodenum leads, through reflexes arising in the latter, to the closure of the pylorus, preventing temporarily a further escape of gastric contents. This gastric juice within the duodenum, until neutralized by those secretions, stimulates the secretion of pancreatic juice, bile, and succus entericus; thereupon the pylorus again opens and the rhythmic movements of the stomach expel a further portion of the gastric juice into the duodenum, which, in turn, leads again to the closure of the pylorus. While the so-called "duodenal reflex" described by Cannon has been questioned by Carlson, McClure and others, it must be recognized that, since physiological function may be attained in more than one way, these earlier investigations are not entirely disproved. This reciprocal action demonstrates the important relation of one part of the digestive apparatus with another. Bayliss and Starling showed that the presence of acid gastric juice in the duodenum stimulates the secretion of *secretin*, a substance which, passing into the blood and reaching the pancreas, excites in that organ its specific secretion; so it would seem that the intermittent and regular discharge of acid gastric juice into the duodenum is indirectly the normal stimulus of the pancreatic secretion. Trypsin, formerly supposed to be a secretion of the pancreas, has been shown by Pawlow and his students to be the result of the action of a substance found in the succus entericus, known as enterokinase, acting upon trypsinogen, which is secreted by the pancreas.

Attention has been called to the fact that psychical conditions may influence salivation and gastric secretion; then there follows stimulation or depression of the motor activity of the stomach and intestine, of the secretions of the duodenum, the pancreas, and the liver.

The impulse starting in a psychic state does not end in its effects upon the liver and pancreas. The functional activity of the small intestine is greatly influenced by the presence therein of the right proportion of secretion from the liver, pancreas, and other glands, and intestinal digestion would suffer in case of decrease or derangement in this supply. Under such conditions irritation of the intestinal mucosa, disturbance of its motor function and lowering of the resistance of the part would result. With such a state of affairs it would be expected that bacterial life, especially within the gut, would be multiplied, fermentation occur, and infection be facilitated. A familiar illustration is found in the marked systemic intoxication that may accompany even a mild inflammation of the mucous lining of duodenum or colon.

With physiological economy, there goes on in health the absorption of biliary salts and probably other substances by the intestine in order to maintain a proper balance of the organism. When a marked disturbance of intestinal digestion exists we have reason to suppose that it interferes with this absorption. While the liver may be embarrassed through not receiving by way of the portal circulation the usual supply of recovered substances, it suffers at the same time because of the absorption of the products of putrefaction or fermentation. It has been shown by Adami that living bacteria reach the liver from the intestine. When the liver is thus overtaxed, a general toxemia supervenes, the whole body is injured, and hemolysis is often exaggerated. There exists a remarkable, although somewhat obscure, relationship between the liver and the kidneys, and under conditions described, renal elimination may be decreased or otherwise deranged. To these evils others may be added when the colon suffers in turn. Delafield emphasized the frequency of chronic colitis as the result of interstitial nephritis, and others have recognized the injurious effects of colitis upon the kidneys.

Relatively great importance attaches to the pylorus, duodenum, cecum, sigmoid, pancreas and gall-bladder. A fuller acquaintance with the functions of these organs not only throws light on the clinical course of the digestive diseases, but serves to warn us that surgical intervention must take into account the possible harm from any great disturbance of the relations of these parts.

4. **Adaptability and Vicarious Action of the Digestive Functions.**— We are impressed by the facility with which one portion of the alimentary tract is able to dispense with the assistance which it ordinarily receives from another, and by the success with which Nature adapts herself to the absence of the function of the stomach and of large portions of either the small intestine or colon. With complete atrophy of the gastric mucosa, or with the bile diverted through a fistula from its intestinal course, or with the pancreas made practically functionless through chronic inflammation, the patient may survive and maintain a moderate degree of general nutrition. The loss of the function of a single digestive organ may not be accompanied by as serious results as ensue from lowering of vitality in the apparatus generally, such as follows grave diseases of the nervous system, or the chronic intoxications and infections. The organ-

ism seems capable of sustaining almost in entirety the loss of function of certain of the digestive organs. Nutrition usually fails as the result of depression, affecting all parts of the apparatus at one time. But it would be a misapprehension to suppose that health can be perfect after the loss of function of any one of the important digestive organs, or after the removal of parts, as, for instance, the stomach.

5. **The Relatively Great Importance of Motor Functions.**—Our understanding of digestive diseases has been much advanced by a clear conception of the rôle of motion in health and in disease as compared with that of secretion. It appears to the writer that the importance of motor disturbances of the digestive tract is not yet fully recognized. We find that although Nature adapts herself more or less successfully to the absence or derangement of what would seem to be necessary secretion, she immediately resents marked disturbances of motility, whether there is overexcitation or overdepression. Especially, we find that evil results are brought about by such interruption of motion as gives rise to stagnation of gastro-intestinal contents or the interruption of the flow of secretion from the great digestive glands. In the latter case the mischief is not alone from the retention of secretion but from the results of stagnation and from the infections and intoxications which are thereby entailed. In a sense it may be said that an exception exists in the instance of the large intestine, where, in event of chronic constipation, we observe a considerable stagnation without necessarily serious consequences. This may be explained from the fact that it is the function of the lower part of the colon to retain its contents, and therefore in constipation we have to deal merely with the exaggerated function, going on ultimately to disease. But even here we recognize the evil consequences that result in some instances from even moderate stagnation, for constipation in certain individuals is immediately succeeded by general digestive derangement as well as by important constitutional symptoms. This is especially true of those unaccustomed to constipation or those in whom there is inadequate activity of the lungs, liver, and kidneys. In relation to the kidneys and liver, this statement is likely to pass unchallenged by some who would doubt its applicability to the lungs, but we probably fail to recognize the full importance of elimination by way of the lungs. Sufferers from emphysema, chronic fibrosis, or continued pulmonary congestion, are strikingly relieved by timely stimulation of the skin, bowels, and kidneys. Doubtless this arises in part through forwarding the circulation and assisting oxygenation, but the practitioner may convince himself that the element of elimination must also be counted. A warning must be given of the evil effects of the habitual use of purgatives and laxatives. This has only recently come to be appreciated.

The studies of Cannon indicate that our conception of the nature of gastro-intestinal motion has to be revised, and new light is thrown upon certain digestive derangements as a result.

6. **The Nature of Functional Disturbances of Digestion.**—The nature of the so-called functional diseases is best apprehended by studying them along general lines such as those suggested. The tangled symptomatology is easily misunderstood, and, for a long time, the pathology and the

pathogenesis for the most part evaded the clinician. So far as relates to the stomach, a better conception of the facts followed soon after the adaptation of the stomach tube as an instrument of diagnosis. It was then seen that the complex of symptoms formerly described as "indigestion" was not a single pathological entity, that it was in fact not one thing but a varied derangement of gastric activity, the more or less direct result of irritation or depression of the sympathetic system. The nature of this action, as shown by Carlson and others, is more complicated than appeared from the work of Eppinger and Hess. These functional affections were early divided into two classes: first, functional disease from excitation, and second, from depression. This division, though useful and at times helpful, is not so simple as it appears; for in not a few patients we may discover evidences of an irritative character at one time and of a depressive at another. Symptoms from excitement may not materially differ from those following depression, and both may be manifestations of physiological fatigue, whether arising from particular or general sources of exhaustion. These different manifestations were soon divided into three classes and termed disorders of secretion, motion, and sensation. Now, while this is a natural and probably permanent step in classification, it must be materially modified and supplemented to make it of value in the understanding of the actual disease. True, we do occasionally meet with a disturbance that seems to be wholly motor, secretory, or sensory; but, with few exceptions, we find a complex in which two or all of these divisions of symptoms occur.

The trend of events that make up a definite and more or less con stant gr oup is to be recognized, and the complex identified and named onlyafter a careful study of the situation. This study must not be limited to the mere investigation of the functional behavior of the stomach. Commonly, the etiology of the trouble will be found in some remote and perhaps unexpected region, in some leak of general energy, if the expression is permissible, or in some undiscovered irritation of the nervous system. Thus a retroverted uterus, proctitis, or a displaced kidney may indirectly lead to important digestive disturbances; even more frequently the cause of gastric asthenia is to be found in eye strain. This subject has been so widely discussed in America, and from so many points of view, that it is somewhat threadbare; yet its signal importance remains largely disregarded. Irregular or asymmetrical astigmatism is the visual defect most often responsible for the functional disturbance, but it is not always in astigmatism of high degree that the trouble arises. It is more commonly found in instances of moderate degree of astigmatism with axes differing in the two eyes, especially in anisometropia. Although not limited to that period of life, the nervous disturbances following these visual defects are apt to appear after the age of maturity, and are especially active when the crystalline body begins from age to lose in pliability. We are indebted to Gould for insisting upon the reality of the matter.

Formerly our text-books referred to but few gastric disorders save the well-established structural processes. With the advent of newer methods of study there arose a tendency to multiply the number of gastric neuroses until the array of titles in a modern book on stomach diseases becomes

bewildering. Undoubtedly much good has come from this minute investigation of functional disorders of the stomach. It has added to our knowledge of the physiology, but now that so many years of conscientious work have been paid out and so many valuable facts have been gathered in, we are in position to review the material along the lines that experience and a sense of proportion would direct.

When this has been well done we shall doubtless agree that our conception of stomach troubles has undergone an absolute reconstruction since the days when text-books treated of "indigestion" and "flatulent dyspepsia;" but we shall admit also that there has been something of over-refinement in the classification, description, and management of the gastric neuroses. It is rather remarkable that this outgrowth of recognized gastric neuroses should have occurred during an epoch in which a basis in definite morbid anatomy was required of practically all diseases; and at a time when if no structural abnormality was shown to bear a constant relation to a symptom-complex, the pathogenesis of that disease was held in doubt. Notwithstanding this, our assembly of nervous affections of the stomach, for which no morbid structural setting was found, was adopted into our nomenclature and was not disputed by most of our clinicians.

Hereafter, as now, we shall doubtless admit that this was a decided advance; but already we are discovering that we had in several instances misconceived the real meaning of the situation. In accepting the doctrine that we might have an array of motor, secretory, or sensory disturbances merely as the expression of a neurosis, we became too oblivious of the fact that this supposed neurasthenia might in fact rest upon some definite local disease that escaped detection.

7. **Functional Disturbances in Relation to Structural Disease.**—This oscillation of opinion that makes for a resting in the truth has come in part as a result of the surgical treatment of abdominal diseases. It was seen that after the removal of gallstones and the drainage or excision of the gall-bladder, not a few of the supposed neuroses promptly disappeared, and the physician who had rested satisfied with the diagnosis of hyperchlorhydria was disconcerted. Gastric derangement is now recognized as a common manifestation in appendicitis and other structural diseases of the lower digestive tract. We are aware that from such causes arise gastric hyperesthesia, hyperchlorhydria, and hypersecretion, besides the syndrome of transient pyloric obstruction with characteristic delay in emptying the stomach even amounting to food stagnation. This latter event may be encountered in cases in which there is no structural narrowing of the pylorus or duodenum, but merely a reflex or spasmodic affection of the pylorus, with or without coincident derangement of gastric secretion, but, necessarily, with serious digestive disturbance both in the stomach and duodenum.

We have long known that this train of events was a natural accompaniment of pyloric or duodenal ulcer. Now that cholecystitis, appendicitis, etc., are admitted as causes, there is difficulty in persuading some men to believe that pyloric spasm ever occurs as the result of a neurosis; on the contrary, they hold that there is always local irritation in the region

of the pylorus. They affirm the local cause and leave the burden of proof with those who yet hold the position that there remains a proportion of cases in which the functional element is the only and sufficient cause. As the evidence in support of this opinion has a fitting application to other supposedly functional disorders, it may be profitably mentioned.

To begin with, only a neurotic origin has been able to explain some of the reported cases of hypertrophic pyloric stenosis. In infancy this curious disease usually does not appear until the lapse of several days or weeks of apparently normal functional activity of the pylorus. The disorder is often congenital, a statement that finds support in the fact that it occasionally develops in twins. However, hypertrophic stenosis may first appear during adolescence or later. The spasticity and muscular overgrowth may occur either in the circular or longitudinal muscle layer, or coincidentally in both. The fact that patients have been cured through the practice of duodenal feeding by Einhorn's method is indicative of the functional nature of the trouble. It is not infrequently associated with cardiospasm and spasticity at the level of the cricoid; globus hystericus may accompany cardiospasm. Attention is drawn to the fact that abnormal contracture especially occurs in those parts of the alimentary canal where there is anatomical narrowing with intermittent contraction and relaxation; at the cricoid, the cardia and the pylorus. All these parts embryologically come from the fore-gut.

There is the analogy of spasm in the sphincter portion of other organs. Cardiospasm, with idiopathic dilatation of the œsophagus which Meltzer elucidated, is an example, to which may be added vesical and anal spasm, besides the involuntary contraction in laryngismus, vaginismus, etc. Still further evidence is found in the cure of these morbid contractions by measures directed solely toward calming excitability. Finally, the surgeons have learned the futility of attacking neurotic affections by operative measures, for, with certain notable exceptions, the symptoms not only continue, but often increase thereafter. That there may remain some hidden structural defect is possible, but, in the light of ascertained facts, improbable. Indeed, when we come to analyze the cases of pylorospasm secondary to a diseased gall-bladder, it will be found that some of them present no signs of former perigastritis nor extension of inflammation to the pylorus or duodenum. In these very cases, then, we must admit some indirect functional excitation, differing, it is true, from our conception of a neurosis but leaving something that morbid anatomy fails to explain. This functional nerve excitation may be comprised in the principle of increased reaction in certain individuals, or in any individual at some particular time, to stimulation in some instances of the nerve fibres of the vagus and in others to stimulation of the fibres of the sympathetic proper.

An unprejudiced view would seem to grant that a disordered nervous system may at times give rise to cardiospasm or pylorospasm, but the warning should be kept in mind thar we should seek the cause in some marked irritation at or near the abnormal contraction.

8. **Structural Changes Resulting from Functional Disorders.**—Accepting the doctrine that many gastric disturbances arise from nervous

causes with and without assignable irritation at some point remote from the stomach, the question occurs as to how far it is possible for structural diseases of the stomach to result from severe or prolonged insult to the nervous system. The belief has long been held that gastric atony and even dilatation may ensue from long-continued nervous depression. It is not difficult to explain gastrectasis as the result of pyloric or upper intestinal obstruction, but there is a large residuum of cases of dilatation in which no obstruction is found, and their origin is usually attributed to prolonged nervous depression and overtaxation of the stomach with resulting myasthenia. In this connection it is interesting to note the accumulation of cases of acute dilatation of the stomach following surgical procedures. These are not limited to abdominal operations or injuries, for there are well-authenticated cases which have developed after extensive injury to one of the extremities or joints, with pneumonia, or accompanying acute tuberculosis or carcinoma. In a proportion of these cases a real obstruction is found, usually in the duodenum, occasioned by compression of the gut between the root of the mesentery and the spinal column, producing acute ileus, the result of dragging of the intestines downward which sometimes occurs in great relaxation of the abdominal wall. In a majority of cases no cause save nervous shock has been discovered.

An important lesson is to be learned from these cases. That gastric and duodenal dilatation can occur within a few hours, with manifestations so serious that death usually results unless proper intervention is resorted to, and that this can occur without any preceding injury to the stomach or other abdominal viscera, seems a striking illustration of the relationship that exists between innervation and the well-being of the digestive apparatus. Until autopsy becomes more general, we are not likely to know what percentage of unexpected fatal terminations after surgical operations may depend upon this accident.

If acute gastrectasis can arise from great depression of visceral innervation, it is conceivable that depression of lesser degree and long continuance may result in atony; and if to this we add the element of overtaxation of the stomach from indiscreet eating, we may easily explain those cases of gastric atony which do not result from obstruction.

One who has had wide experience in the examination of gastric contents is aware of the striking influence which the state of the nervous system has upon gastric secretion. It is not uncommon to find instances of hyperchlorhydria which disappear as soon as the patient follows a quiet, orderly life. On the other hand, systematic rest, with consequent improvement in the general health, often leads to the return of normal secretion in hypochlorhydria. In many instances it will be found that the neurasthenic state that gives rise to the gastric symptoms may not depend upon inherited weakness nor upon general nervous exhaustion, but rather upon the overfatigue of some particular part of the nervous system. Mere local treatment of the stomach unaccompanied by improvement in other directions is usually unsuccessful in inducing a cure.

One naturally inquires whether these long-continued disturbances of secretion may not lead to inflammatory and other lesions of the gastric

mucosa. Gastritis has rightly been given extensive consideration in most treatises on stomach diseases, though according to the experience of some, its frequency is exaggerated. The disease is to be regarded as an infection of the stomach. One is impressed, however, with the truth long ago pointed out by Beaumont, that the recuperative and regenerative power of the gastric mucosa is remarkable, and we find that not only inflammation, but moderate trauma of the stomach, goes on to rapid repair, provided the general conditions are favorable. What is often regarded as gastritis is in fact a functional irritability of the stomach lining, a hyperesthesia gastrica, and not a true inflammation. In the extremes of age or when resisting power has been greatly reduced by long-continued fatigue, general infection, or great nervous depression, experience shows that gastritis is readily excited and that, when once present, it is likely to continue until the general health is improved. This is also true of the gastric neuroses, and just as hyperesthesia and motor irregularity may be caused and continued by systemic depression, so also may this be true of gastritis. Apparently a good deal of confusion exists in the mind of the average practitioner as to when a case is inflammatory and when it is merely one of functional irritability. It is important to make the differentiation, but it is occasionally difficult, as also is the recognition of the etiological factors upon which either affection is based. While it is understood that a functional disturbance may arise as a result of nervous depression or excitement, that gastritis may depend upon such depression is not sufficiently recognized.

One must not dwell too much upon systemic depression as a cause in the development of gastritis; it is only a factor which predisposes to infection. It is commonly and justly believed that the toxemias also invite gastritis. This probably results from a lowering of vitality in the gastric mucosa such as the intoxications may induce in other tissues. Local disturbances like acute constipation, hepatic congestion, and overloading the stomach are factors which generally aid in setting up this inflammatory reaction. The point should be made that while one person easily withstands indiscretion in diet, another immediately suffers from gastritis, and this is true because of the lowered resistance to infections which exists in certain individuals, a truth paralleled in infections of other organs; thus some individuals are predisposed to such infections as appendicitis, colitis, and cholecystitis.

9. **Structure and Function in Relation to Peptic Ulcer.**—In the search for the etiology of peptic ulcer we have discovered a number of other things, but not precisely that, and the ground has been so much tramped over that the boundaries of the question are considerably obscured. It is highly probable that though we include in one group cases found postmortem, those produced experimentally, and those recognized clinically, they are not necessarily exactly the same thing. Gastric ulcer has been produced in animals experimentally by prolonged feeding on infected food. Inferentially, the same result would obtain in man; nevertheless, except when stagnation exists, the stomach with peptic ulcer is remarkably free of the usual evidences of infection. Virchow apparently solved the problem by the hypothesis of thrombus, and this cause has been shown

to explain rare cases, though it apparently has no place as a cause in the great majority. A like conclusion attaches to the theories that gastric hyperacidity, lowered alkalinity of the blood, local trauma or the accidental manifestations of other diseases, like tuberculosis, syphilis, scurvy, or diabetes, are the direct and single cause. That the gastric mucosa may suffer ulceration like other surfaces of the body and from identical causes will probably not be disputed, but it is scarcely justifiable to regard all these instances as peptic ulcer.

If we consider the method of development of peptic ulcer we perceive two things, namely, gastric hyperacidity and lowering of vitality of tissue at a circumscribed point; we fail to account for the special cause that may explain the devitalization of tissue at these points. We should consider the following facts: (1) Classical acute peptic ulcer is prone to occur in chlorotic young women, and, although the exceptions are many, the rule must not be obscured. (2) Classical chronic or indurated peptic ulcer is prone to occur in men past middle age. (3) Peptic ulcer is prone to localize itself either at the lesser curve on the posterior surface near the pylorus, or in the duodenum. (4) Its tendency is to continue, to become chronic. (5) Some ulcers show immediately a design to perforate, others seem forever limited to the mucosa. In acute ulcer the secretion of very acid gastric juice is usually present.

In reviewing these special features we recall unquestioned instances tending to nullify the rule; but too much weight should not be given to the exceptions in a subject holding so many possibilities of confusion; we should rather attempt to trace the usual lines more deeply, while at the same time noting and interrogating the unusual. After doing this it would seem clear that in the gastric ulcer of the dead house we are dealing with several entities—differing in cause, tendency, history, and termination—although there are certain manifestations in which they are alike.

It would seem that there is some as yet unknown factor at work in the cause of true peptic ulcer, some factor which lowers the vitality of tissue, especially in certain regions of the stomach and duodenum. Apparently this factor is relatively common in early adult life in women, and after middle life in men, and in the latter is more disposed to chronicity. What is this factor? Will it be found in the local deficiency of antibodies, as suggested by Weinland? In local ischemia? In preceding lesions of neurotrophic nature, analogous to herpes or to the perforating ulcer of the integument? These questions remain unanswered, and the operative treatment of gastric and duodenal ulcer, while proving that the disease is more frequent than we were prepared to admit, and showing that, in men, duodenal peptic ulcer is seen about as often as gastric ulcer, has not materially aided in explaining the nature of the process. The hypothetical disappearance of antibodies may well account for the loss of tissue, but how shall we explain the local deficiency in antibodies? May this not rest in the neurotrophic realm?

Whatever may be the exciting cause, we are reasonably certain that the increased activity of the gastric secretion and its overacidity contribute much toward the rapid evolution of the ulcer and toward its

chronicity. The pain and gastric irritability are to be explained in part by the pyloric and gastric spasm and by the delay in the onward passage of chyme. Thus, the rationale of the usual medical treatment by rest, diet, alkalis, local sedatives, and external applications is made evident. When failure follows this treatment, the result would seem to be attributable largely to the fact that it requires the utmost attention and pains to prevent interruptions in the course of treatment, and that a short interruption may prove sufficient to overcome what has been gained by days of patient effort. Whether food is denied or in proper form is given frequently and persistently, the idea of keeping the gastric acidity low and overcoming the element of spasm must never be forgotten; even after gastro-enterostomy done to procure drainage, the benefit resulting from a modified diet and a lowered gastric acidity is of considerable importance.

By a control of the functional activity of the organ we are able to modify the course of the structural disease. Of course, this principle is not limited to gastric ulcer, but illustrates the important and persistent interrelation that exists between organs and functions. Perhaps we should be more earnest in tracking structural diseases to a starting place in functional derangement, to the finding of lowered resistance in some areas of tissue as the result of biochemical deficiency, possibly neurotrophic in its inception. All this may strike some men as lacking the evidence of acknowledged experience, but such a decision would be premature. There are many facts to be marshalled in its support.

We observe herpes facialis, sometimes persisting for weeks, appearing in some individuals whenever the health is depreciated by fatigue or other general causes. Such eruptions are prone to attack a certain area, reappearing in the same place and occasionally accompanied by severe pain. We occasionally observe perforating ulcer of the arm or leg persisting indefinitely, resisting topical treatment and recurring after excision. We should recall Raynaud's disease and also the curious non-traumatic hematoma auris, particularly observed in the insane. Marked subcutaneous extravasations of blood appear in certain neurotics in various parts of the body, disappearing, then recurring after a period of health. In one patient the writer observed this at intervals during several years; the attack sometimes alternated with, sometimes were accompanied by, the classical symptoms of gastric ulcer, and occasionally by hematemesis of grave character. In erythema multiforme one may observe the wide involvement of the mucous membrane, and one severe case was observed in which this disease was accompanied by the symptoms of gastric ulcer. This collection of presumably neurotic affections associated with structural lesions shows an indubitable relation between the nervous system and the integrity of tissue.

We have insufficient experimental evidence to prove that either a nerve lesion or a neurotrophic disturbance is a frequent cause of peptic ulcer, but the behavior of the affection strongly suggests the possibility. These statements are intended to emphasize a principle that seems to be too little recognized, that of the very close relationship existing in all parts of the organism between the structure and the functions which utilize that structure. It is true that we often find a structural change

to explain the supposed functional disturbance, but it seems equally true that the functional disturbance may be the forerunning etiological factor in, sometimes the cause of, the structural disease.

Much has been written on *focal infection* as the chief etiological factor of peptic ulcer. Rosenow's work shows that gastric ulcer may be excited by inoculation with special strains of micrococci, often derived from infected teeth or tonsils. It is an interesting fact that individuals prone to attacks of herpes may lose this predisposition when a source of infection has been eliminated. Without accepting the doctrine that focal infection is the common cause of peptic ulcer, most clinicians, nevertheless, are quick to remove all discoverable sources of focal infection. In this connection the possible effect of allergy should be considered.

The hyperchlorhydria so commonly present in peptic ulcer is often intensified by food retention, secondary to pyloric spasm, and the same cause is responsible for some cases of that condition usually called gastrosuccorrhœa. However, there are cases of excessive secretion in which hyperchlorhydria is not dependent on spasm. It was long believed that this might be produced by local stimulation occasioned by the open ulcer. Pawlow's observations tended to discredit this view. He failed to excite gastric secretion in animals by irritation locally applied, although juice flowed freely at the sight of food and upon its introduction into the stomach. A highly acid secretion is made to flow in dogs as a result of faradization of the mucosa. A. Schiff was able to excite the flow of gastric juice by local stimulation when the factor of psychic effects and the presence of food in the mouth or the stomach were eliminated. Clinically, we find that the acidity is increased by feeding and even by the suggestion of eating. But we also know that hyperchlorhydria is present in gastric ulcer even when the patient is fasting and when psychic influence is wanting. It is probable, therefore, that gastric secretion is excited by the irritation of an ulcer as well as by the suggestion or presence of food.

One may conclude that there is usually an excessive secretion and at times retention of gastric juice in this disease, and there can be no doubt of the unfavorable effect of hyperacidity on the ulcer. Further, we know that anemia, often associated with ulcer, is generally accompanied by hyperchlorhydria, and that an impressionable nervous system at least predisposes to the oversecretion.

10. **The Question of Secretion.**—The behavior of the stomach in the matter of secretion presents a problem not yet elucidated. By the action of certain proteins upon the mucosa of the pyloric end of the stomach there is excited in the glandular structure of the part a substance which passes into the general circulation, returns to the gastric mucosa, and excites therein an active secretion of gastric juice. Pawlow and Popielski showed that this secretion occurs after the destruction of all nerves connecting the stomach with the ganglionic centres. Edkins showed that it is not the result of a local reflex in the gastric walls, but is owing to a chemical influence. It is interesting to discover that the secretions of the stomach are governed by influences other than psychic or reflex nervous mechanisms. The facts lead us to conclude that gastric secretion may be stimulated by psychic influence, by direct stimulus

occasioned by food in the stomach, and, finally, by the specific action of some chemical substance formed in the pylorus and acting through the pylorus and acting through the blood upon the remaining portions of the mucous membrane of the stomach.

We still await the application of these physiological findings to explain certain clinical conditions. Although many cases of so-called gastrosuccorrhœa are in reality but instances of retention, there remains a group exempt from stagnation, but in which, although the stomach is washed out at bedtime, a considerable amount of gastric juice is found in the fasting stomach in the morning. Sometimes the secretion is so excessive as to lead to morning vomiting; in contrast is achylia gastrica, in which no secretion can be discovered. Some patients who suffer from hypersecretion suddenly, and so far unaccountably, experience a diminution or suppression of secretion; in other words, a patient who one day is an example of hyperchlorhydria, on the succeeding day or week shows a continued absence of hydrochloric acid free or combined. When gastric secretion is for a long time absent, we describe the condition by the term "achylia gastrica." This affection, frequently seems to be unrelated to any morbid change in the structure of the gastric mucosa. In prolonged cases the glandular structure undergoes atrophy, and restoration of secretion becomes impossible.

It would be easy to explain these cases by inflammatory or degenerative processes in the mucous membrane of the stomach, but such conditions are apparently absent in the early stages of a large proportion of cases. At times the disease is susceptible of satisfactory improvement following local stimulation and general treatment; but often the trend of the disease is toward permanent loss of function. Lacking the stimulus of the free hydrochloric acid, the pylorus does not contract firmly, and the unchanged gastric contents pass into the duodenum, sometimes very soon after the meal is eaten. In such cases the stomach will be found empty an hour after the ingestion of food, or if the stomach tube is employed soon enough to regain the stomach content, it is found to have undergone no digestive change except such as depends upon the action of the salivary ferments. Since we have come to look upon the proper quantity and quality of gastric juice as the normal stimulus of duodenal digestion and as the signal for secretion in the pancreas, liver, and intestine, it is difficult to understand how patients suffering from achylia gastrica can continue in fair health and with moderately good general nutrition. Such however, is sometimes the case. Patients with achylia gastrica followed for fifteen years, while never well, are yet not materially worse than at the beginning of the observations. The recent experimental work of McClure may throw light on this subject. In some instances there was apparent improvement which coincided with pregnancy and disappeared as soon as the period of lactation had passed.

On examination of the stools of patients with achylia gastrica, although it is common to find that too great a proportion of the food is passed undigested, and although probably a certain amount of it has undergone disintegration through the action of bacteria, still it is evident that the patients digest and assimilate a reasonable proportion of food, as they

are able to maintain their weight at a somewhat lower standard, and to develop a fair, although diminished, energy. We have in the recent accounts of the physiology of digestion an explanation of certain of the phenomena in achylia gastrica, but we are embarrassed in that they explain too much. The victims of achylia gastrica suffer far less than should be expected.

It would appear that some of the secretions are activated through stimuli with which we are unacquainted, as otherwise it is difficult to explain the comparatively good health which many patients enjoy after closure of the pylorus associated with gastrojejunostomy.

It is interesting in this connection to consider the question of natural and artificial inhibition of peptic digestion. There are cases in which despite high acidity of the gastric content, depending upon free hydrochloric acid, proteolytic digestion does not proceed; something has blocked the digestive process. The explanation of this inhibition has been sought for in various directions. Apparently there are some natural causes of inhibition, perhaps depending upon the stomach itself through the formation there of antibodies. But certain foods and drugs also exercise an inhibitory action on digestion. The albumoses, gelatin and maltose, for instance, have a definite inhibitory effect, while lactose and most carbohydrates have none. In certain instances the concentration of the gastric juice interferes with the digestion of proteins as well as other foods, and when the secretion of the stomach is diluted the digestive process is apparently favored. These facts may account for the curious behavior of the gastric digestion often observed clinically; the amount of free hydrochloric acid may be above the recognized standard and yet digestion does not proceed. In reviewing the question Sailer concludes that, after attributing to certain foods and drugs the power of inhibiting gastric digestion, and admitting that the element of concentration under special conditions operates to produce a like effect, there remains a group of facts that may be best explained on the hypothesis of the presence of an antipepsin such as has been announced by Danielewsky and Weinland. This substance may have a role, not only in protecting the walls of the stomach, but also, in certain conditions, of inhibiting proteolysis in the gastric contents.

With long-continued achylia gastrica, a certain proportion of patients show very defective intestinal digestion. In other cases the intestinal digestion seems satisfactory, and we are forced to conclude that besides the acid secretion of the stomach there must be some other agent that stimulates the production of secretin. Whatever this agent may be, its presence is more manifest in some cases than in others, if we are to explain thereby the variations in the intestinal digestion in cases of achylia gastrica.

Another important matter relates to disturbances in metabolism especially when this involves functional disturbances of the liver. Careful examination of the stools shows that there is a wide variation in the amount of biliary coloring matter discharged in the intestine. The study of the secretion of the bile, so far as can be judged, confirms the belief that at least one function of the liver shows considerable change in activity

from time to time. From the evidence we may conclude that these temporary modifications of hepatic function are directly influenced through the nervous system, through psychic impulses, excitement, fatigue or depression. Drugs have comparatively little effect on the secretion of bile, apparently more upon metabolic processes, but the state of the nervous system seems to be potent in this regard. The secretion of bile is stimulated by the administration of biliary salts and in a somewhat less degree by the taking of oils. Stimulated by a suggestion of Meltzer, applying his law of "contrary innervation" to relaxation of the biliary tract, Vincent Lyon has devised a system for promoting biliary drainage that gives practical results in the diagnosis and treatment of diseases of the liver and bile pasages. The withdrawal of bile through the duodenal tube and the study of its characteristics, in connection with the use of magnesium sulphate or olive oil, gives valuable information concerning the biliary tract. Though the method is not to be too arbitrarily interpreted, it is of real use as an aid in the correct understanding and treatment of many biliary disturbances.

11. **Infection in Relation to Digestion.**—The importance of recognized infection in the etiology of structural diseases of the liver and biliary apparatus leads to the suspicion that unknown infections of moderate activity have much to do with the variations of functional power of the liver that are commonly ascribed to other causes. It must be owing to an acquired or inherent resistance that the liver is not more markedly and frequently deranged than it is by the occurrence of an unwholesome condition of the gastro-intestinal tract. Clinical experience leads to the conclusion that the constant presence in the intestine of pathogenic microörganisms and other sources of intoxication, which may not materially disorder the economy, must be tolerated by means of some form of immunity. It is further observed that with unusual nervous depression this protective barrier of immunity becomes insufficient; the symptoms of toxemia result, and not infrequently those of infection as well.

Undoubtedly these manifestations are not confined to the liver, for we perceive similar occurrences in the parenchyma of the stomach and intestine in gastro-enteritis. It can scarcely be an error to infer that organs that are thus intimately correlated and thus largely influenced by the sympathetic nerves must react to untoward nerve influences; and under such circumstances, when, so to speak, "the guard is down," the infection most readily breaks through and toxins still further disturb the function. We may find illustrative examples most often in young children, as in the effect of fright, injury, or heat exposure.

Late work indicates that infection starting in the alimentary canal may pass through the portal vein and lymphatics to the liver and produce disease in liver parenchyma and biliary tract. Disease of the gall-bladder is thus seen to be less an entity than was once believed to be true.

12. **Visceral Blood Supply in Relation to Digestion.**—Resistance to disease by the liver seems to be proportioned in a measure to the liberality of the blood supply, and fails when, from narrowing of the hepatic artery, the supply of oxygen is decreased. While it is impossible to measure the precise responsibility of each factor that operates in the development of

the morbid process, it is evident that weight must be given not only to that which circulates in the blood, but to the volume of blood as well; and for this reason more thought has been given to the question of sclerosis in the abdominal aorta and its branches.

Years ago it was suggested that in case of unusually large and numerous inosculations of the branches of the portal vein with the systemic veins, a sufficient auto-intoxication to produce definite symptoms might result. The explanation of coma in hepatic cirrhosis was adduced as an illustration. The introduction of epiplopexy enabled us to observe effects of such inosculations artificially produced, and it must be admitted that some justification is found for the claim that toxic effects may be induced in this way. Especially is this true before the organism has accommodated itself to the change in the circulation, and presumably, also, when the portal blood is for any reason in a specially toxic condition.

Not alone the liver may be the victim of these vascular defects, but also the other abdominal viscera. Thus some forms of pancreatitis are to be explained, and not a few instances of that disease of multiple etiology, colica mucosa. Arteriosclerosis, aortitis, and peri-aortitis abdominis may be held to account for many degenerations, functional disturbances, and special symptoms of the digestive apparatus. Among the latter are included neuralgias, motor disturbances, and lowered secretion. In those free from structural disease of the vessels, troublesome visceral disturbances resulting from vasomotor disturbances may occur. Perhaps certain affections whose origin is attributed to perturbation of the nervous system, and which are called functional, are so in a different sense than that conceived. They may properly be charged to morbid conditions of the vasomotor centres.

This would seem to be true especially of *mucous colitis*, an affection that has been accounted for by many morbid processes, some of them opposite in nature, but all perhaps possessing in common the quality of excitement or depression of the blood supply through disturbance of vasomotor centres or through more direct influence, and hence leading to prolonged congestion or ischemia of the colon. What is true in this part of the intestine may well be so in other parts and other organs. Vasomotor disturbance is an old conception, long used to explain visceral diseases, and although this view has been carried to extremes, it has never been quite dislodged, and undoubtedly, in a proportion of cases, is a source of trouble.

Passive congestion of the abdominal viscera at once induces a lowered functional activity and later degenerative structural changes. At first there is depression of the specific secretions with an increased activity of the muciparous glands. The motor function of the stomach and intestine becomes hesitating, irregular, and feeble, discomfort or distress is experienced, digestion is delayed and imperfect, while an exuberant growth of bacteria leads to increased toxicity of the gastro-intestinal contents. A lowered resistance of the tissues favors the entrance of pathogenic microorganisms and the setting up of inflammatory changes of a low order which, with the assistance of an increased toxicity, account for the

degeneration of the parenchyma and the growth of connective tissue in the digestive organs in prolonged portal stasis.

13. **False Combinations of Secretion.—Disharmony.**—The interrelation of the secretions, the enzymes, and activating substances is complex but interesting. By conjoint action they apparently lead to amazing results, and some of these still remain incomprehensible. There are both clinical and experimental reasons for believing that disharmony in physiological reactions may result in profound disorder of the digestive organs and even in the most serious organic diseases. Perhaps no better instance of the latter can be pointed out than pancreatitis induced by experimental injection of the duct of Wirsung with bile or with artificial gastric juice. Undoubtedly certain cases of pancreatitis follow obstruction in the ductus choledochus at the ampulla and the escape of bile into the pancreatic duct. Possibly the more acute cases may ensue from the entrance of gastric juice into the pancreatic channels passing from the duodenum. This seems more probable in light of the work of H. U. Williams. He shows that gall-stones may so far dilate the outlet of the ductus choledochus as to make easy the entrance of duodenal contents, including bacteria and chemical agents, which might thus find their way into the pancreas. These dramatic and antagonistic results of misplaced physiological secretions seem in part to be demonstrated by the relief observed to follow the drainage of the biliary tract in chronic pancreatitis. There are doubtless other instances of injury inflicted inside the redoubts and not by the enemy. Some of these we rather dimly perceive, others are undiscovered, yet we see their results.

14. **The Place of the Biliary Tract in Digestive Pathology.**—The gall-bladder is a prolific source of disease in the abdominal organs. A great proportion of diseases of the gall-bladder result from infection, a statement which applies with equal force to the various forms of cholangitis. Without entering into the discussion of the means by which microörganisms find entrance into the bile passages, we find them present there, and as a result, an inflammation of greater or less severity is often established. The more acute infections give rise to suppuration or necrosis of the gall-bladder, while the milder ones set up an inflammatory œdema of the lining mucosa, and thus embarrass the natural ebb and flow of bile. The lining of the gall-bladder is not destroyed, but is irritated, and, as a result, an excess of cholesterin is secreted and the changed condition of the bile contained in the gall-bladder leads to the formation of calculi, in the centre of which, if the stones are recently formed, colonies of bacteria may be found. The conditions which seem most favorable to the enlargement of a biliary calculus appear to be a slight inflammation of the lining of the gall-bladder with temporary and recurring obstruction to the cystic duct. Under these conditions the stone is likely to increase by laminated formation, and its presence in an irritated gall-bladder may excite spasm of its walls, which induces the symptoms known as hepatic colic.

The inflammation of the biliary apparatus and the increased tension put upon it lead to more or less permanent changes, such as dilatation of the biliary canals, widening of the outlet of the choledochus, and inflam-

matory adhesions uniting the gall-bladder to the surrounding parts. Concurrent with these events there is usually much sympathetic disturbance of other viscera sometimes so marked as to distract attention from the original seat of trouble. With the biliary apparatus crippled future infection is facilitated, and recurrence of cholecystitis and cholangitis is frequent unless the patient acquires an immunity through improvement in the general health. Diathesis is an important factor in disturbing immunity and diathesis is closely related to metabolic peculiarity. When protein or carbohydrate metabolism is faulty, infection occurs more readily and to successfully oppose it special attention may be required as to diet and elimination.

15. **Some Peculiarities of Pancreatitis.**—There seems to be a definite relation between disease of the biliary apparatus and pancreatitis. There is accordingly a belief that this disease, whether acute or chronic, follows upon the entrance of infectious microörganisms through the duct of Wirsung. While this is doubtless true in some cases, there are instances of acute hemorrhagic pancreatitis in which no infection is demonstrable, despite careful search. It is recognized that the destruction of the gland and the production of fat necrosis, so often an accompaniment of the acute forms of pancreatitis, are definite results of autolysis of the gland structure through the action of its own ferments and the digestive effects of these ferments on the fatty tissues in various parts of the abdomen, and even (through the lymphatics) in other parts of the body. Hemorrhage into the substance of the pancreas occurs at times without trauma, inflammation, or other assignable cause. It remains one of the unsolved questions.

16. **Correlation of the Abdominal Viscera through the Vagus and Sympathetic.**—There apparently exists a relation between the suprarenal glands and the functional activity of the pancreas and liver. The appearance of glycosuria in instances of intoxication with adrenal extract seems to bear on this relation. The abdominal sympathetic and vagal nerves are associated closely with the function of the suprarenals as well as with that of the pancreas and liver. Meltzer found that when the cervical sympathetic ganglion was removed from animals their pupils dilated widely upon the instillation of adrenalin solution. Loewi, suspecting that inhibition of nerve influence might lead, through action upon the function of the liver, to hyperglycemia and glycosuria, and supposing this inhibition to be connected with the pancreas, practised the ablation of this organ. In the animals thus operated on there appeared the usual glycosuria, and, in verification of his hypothesis, when adrenalin solution was instilled in the animals' eyes marked mydriasis immediately appeared. Following this he applied adrenal solution to the eyes of 18 diabetic patients, and of these, 10 at once showed mydriasis. In 28 non-diabetic patients the reaction failed in all but 2. One of these proved to have obstruction of the duct of Wirsung, and the other had Graves' disease.

These results indicate that the functions of the pancreas, liver, adrenal bodies and kidney are closely related through the sympathetic nerves.

Sialorrhœa, as a definite symptom of pancreatic disease, is largely discredited, yet its concurrence must be admitted, sometimes in pan-

creatic calculus, again in cancer of the head, and occasionally associated with transient glycosuria. The reality of so-called pancreatic sialorrhœa should not be too quickly abandoned. By the study of the unusual phenomena we may dispel the mist that obscures the field wherein play some of the most incomprehensible vital processes.

17. **Splanchnoptosis and Overtension of the Peritoneum.**—The displacements of viscera contribute in several ways to derangements of digestion. Gastroptosis may interfere with the motor function of the stomach through increased traction upon its membranous supports, thus giving rise to discomfort as well as interference with the blood supply. The results of displacement of the small intestine are less understood, but ptosis of the colon, including displacement of the cecum and the sigmoid, is not infrequently the cause of symptoms and disease. The shortening of the ascending colon, thus raising the cecum to the upper part of the abdomen, the displacement of the colon downward, the exaggeration of the flexures, and the displacement of the transverse colon downward so that it appears as a long loop, occasionally as a double loop reaching the pelvis, are among the dislocations. Jacobi pointed out that the sigmoid flexure in the fetus is relatively very long, and this disproportion occasionally continues beyond infancy, even to adult life. Another common defect is the extension of the so-called omega loop of the sigmoid to the right until it may reach the region of the cecum. This is occasionally associated with extremely sharp bending of the sigmoid. The displacements of the stomach and the colon are apparently more important than those of the small intestine; at any rate, they are better understood. From excessive angulation of the sigmoid, stasis and dilatation of the colon frequently result. This angulation is also a contributing factor in exciting sigmoiditis, and is a source of embarrassment in the treatment of that affection. It is not appreciated that incomplete hernia is often the cause of more or less continuous abdominal distress and sometimes severe pain which is experienced in regions somewhat remote from the point of irritation. This is seen in the very small epigastric herniæ frequently found in the linea alba, and also in incomplete and unsuspected herniæ of the inguinal and femoral canals. As these symptoms have been repeatedly shown to result from external hernia, it is fair to presume that like results obtain from internal hernia. It is probable that some of the patients who have undergone repeated abdominal explorations, hoping for a discovery of the source of pain and other symptoms, are suffering from unsuspected traction of some part of the peritoneum or intestine which is caused by hernia.

As vestiges of past inflammation, *adhesions* of one part of the peritoneum with another sometimes remain, and the unnatural traction thus induced may so far irritate the peritoneum as to occasion pain and, reflexly, considerable derangement of the digestive processes; or there may be sufficient adhesion of the intestine or stomach to embarrass peristaltic movement and delay the onward passage of the contents. The symptoms thus induced, while of little moment in the more phlegmatic, become important in those hypersensitive beings who are prone to have abnormal abdominal sensation, and in whom a harmonious physiological

digestion is more often the exception than the rule. In such individuals relief is sometimes obtained by judicious medical gymnastics and psychotherapy, while surgical measures rather augment the complaint, either because of the new adhesions formed or because the attention of the introspective patient becomes more firmly fixed on himself.

According to Wilms, the pain occasioned by disease or irritation in the abdominal viscera is really produced by means of traction communicated to the mesentery. The cerebrospinal system of nerves, distributed to the parietal peritoneum, is the seat of most abdominal pain. Some think that the splanchnic and pneumogastric nerves are not implicated, but that abdominal pain is excited only in the endings of the cerebrospinal nerves, distributed to the parietal peritoneum (Lennander). Traction upon the mesentery or upon the adhesions irritates these sensory nerves. Overdistention of a loop of intestine leads to stretching of the mesentery and indirectly to tension of the parietal peritoneum.

From this point of view it is easy to understand how pain may be excited in regions somewhat remote from the seat of mechanical pressure or tugging, as occurs in hernia, adhesions, and visceral displacements.

18. **Psychoneuroses in Relation to Digestion.**—Frequently an association exists between digestive disturbances and the more definite neuroses and psychoses. Long continuance of infection of the digestive tract inducing a lowering of the general nutrition, leads to depression or irritation of nerve tissue, and sometimes appears to be the exciting cause of brain disease and also adds to its continuance. This is shown by the marked improvement that follows an enlightened course of dietetic and other treatment especially directed to the betterment of primary digestion. On the other hand, the lowered vitality, induced by definite nerve disease, is almost invariably accompanied by digestive disturbance. Illustrations of this fact are observed when the nervous disease rests upon inheritance rather than upon long-continued nerve strain. It is probable that infection and toxemia are much concerned in these morbid processes, both nervous and mental. With lowered resisting power from mental disease infection of the digestive tract is easily excited.

Under these conditions the intoxications increase because of accompanying faulty elimination. It is commonly observed that victims of nervous or mental disease suffer from urinary inadequacy, and from depression of the other emunctories. To this may be added the element of faulty metabolism which succeeds upon disturbance of organs of internal secretions, as, for instance, the adrenals and thyroid. Enteroptosis with atony and dilatation of the hollow abdominal viscera is frequently encountered in the neurotic and the insane. Besides, congestion and degeneration of the glandular structures often occur, including the liver and pancreas, as well as the secreting tissues of the stomach and intestine.

19. **Malnutrition and Superalimentation.**—A normal appetite is a Promethean gift and punishment awaits those who profane it. Psychic impulses enhance appetite or, conversely, blunt or extinguish it. Habit and example are potent factors either in skimping the meal or in gluttony. Insufficient eating weakens digestive functions, while excessive eating

tires them. Thus pathological states may spring from continued neglect or abuse of alimentation. Popular misconceptions about eating do harm. Of late a restricted diet is much practised to acquire slenderness. Such a dietary predisposes to tuberculosis and other infections and to neurasthenia. On the other hand superalimentation exposes one to serious metabolic derangements.

20. **Variations in the Intestinal Flora in Their Relation to Diseases of the Digestive Tract.**—The character of the intestinal flora, particularly that of the colon, is a matter requiring careful consideration. When patients are deprived of foods containing animal proteins, remarkable improvement is reported to follow the deliberate attempts to plant new orders of bacteria, the presence of which is antagonistic to those microörganisms more especially concerned in the putrefaction of animal proteins and the incidental production of toxic substances.

To recur to the question of motor insufficiency and imperfect drainage, the importance of which in the clinical course of digestive disease has been pointed out, the matter appears more conspicuous in the light of the bacteriology of the intestine. Indication for attention to this source of trouble may be found in the urine. While certain urinary toxins are the products of metabolism more or less normal, and depend upon the state of the cellular tissues, other urinary toxins develop in the intestine to a considerable extent. The infections of the gastro-intestinal tract occur both with and without inflammation, but in either event they are accompanied by derangements of secretion. Subacute gastro-enteritis may be followed by degeneration of the glandular parenchyma and even by exudation into the muscular layers, followed by round-cell infiltration and subsequent motor weakness of the stomach and intestine.

The evil effects of imperfect colonic drainage, induced by the presence of kinks in, adhesions to, or deformity of the colon, extend to all parts of the economy.

It is because of the similarity in the symptoms between functional derangements on the one hand and of infection and inflammation on the other that there has arisen the confusion in differentiating these conditions. The difficulty is not lessened by the fact that infection is prone to follow certain of the neuroses; in fact, they often co-exist. Lowered vitality of a part favors infection, and then there exists a causal relation between neurasthenia and appendicitis, colitis, or other inflammatory involvement of the digestive apparatus.

CHAPTER VI

DISEASES OF THE MOUTH AND SALIVARY GLANDS

By DAVID RIESMAN, M.D.

REVISED BY

HENRY K. MOHLER, M.D.

A THOROUGH examination of the mouth by all available methods is of great value, not only in the study of diseases localized in or confined to the oral cavity, but also in the investigation of general morbid states. Examination of the mouth is, however, often neglected, probably because so frequently good general health is found associated with a wretched condition of the gums and teeth. But this fact should not make us indifferent to the importance of morbid conditions in the mouth as sources of general disturbance and as features of diagnostic value. A good deal can be learned by a simple routine inspection. The blue line of lead may clear up the diagnosis in an obscure case. The presence of pyorrhœa, ulcerative processes and abscesses may afford a clue to the etiology of chronic arthritis or a general septicemia. Pigmentation of the mucous membrane may suggest the existence of Addison's disease.

A proper study of the mouth comprises inspection of the lips, gums, teeth, tongue, floor of the mouth, salivary glands, and general buccal mucous membrane. In cases of disturbed taste, false teeth and plates should be removed to ascertain their condition and that of the parts with which they are in contact. The sensation of taste should be tested in the accustomed ways; the saliva should be examined as to its consistency, quantity, odor, reaction, and chemical composition. A bacteriological study of the mouth may prove useful. Palpation may often aid inspection. A roentgen-ray examination is necessary in the study of many diseased conditions of the mouth.

Bacteriology.—The mouth is the constant habitat of many bacteria, by far the largest number of which are harmless saprophytes; but there are some that possess pathogenic properties, which they display, either in the mouth or elsewhere, when suitable conditions obtain. If the care of the mouth is neglected, the number and variety of pathogenic and non-pathogenic bacteria increase. The bacterial flora of the mouth is of course derived chiefly from without, from the air, food, and drink; but when infective processes are active in the organs or parts communicating directly or indirectly with the mouth, the bacteria concerned in them may find their way to the oral cavity. Thus in pulmonary tuberculosis, tubercle bacilli may be deposited in the mouth; and the salivary glands are capable of eliminating bacteria circulating in the blood.

Despite the fact that the oral cavity teems with bacteria, wounds about the mouth usually heal by first intention. This is to be explained by the fact that the saliva is not a good culture medium for bacteria, although its bactericidal power is extremely weak.

Aside from individual differences, there is a natural difference between the saliva of the submaxillary and that of the parotid gland. In most animals the first furnishes a secretion that has only a slightly deleterious action upon bacteria; while parotid saliva is capable of inhibiting the growth of several species of organisms. Those of the pyogenic group seem to suffer most in that respect, especially if the secretion is artificially stimulated. When abundantly secreted, the saliva may become sterile.

Many strains and types of microörganisms may be present in the mouth, varying greatly under different conditions. Among the most commonly found are: streptococci, staphylococci, pneumococci, *Micrococcus catarrhalis*, diphtheria and pseudodiphtheria bacilli, streptothrices, yeasts, moulds, spirochetes and many others. Organisms may exist in the body without producing symptoms, and this phenomena can be explained by considering the relation between the body resistance and the infectivity of the organism as being balanced. So long as this equilibrium is maintained, no disease develops. Should the infectivity become enhanced or the resistance of the body be reduced, the balance is altered in favor of the bacteria and disease sets in.

SEPTIC INFECTION OF ORAL ORIGIN

Infection of the teeth, gums, tonsils, pharynx and various forms of stomatitis have been shown to be responsible for a number of systemic diseases and disorders. These structures, when diseased, are foci of infection and are capable of producing lesions in other tissues of the body. The hypothesis which assumes the causative connection between the primary focus and secondary lesion is called the "focal infection theory."

Infectious processes in the mouth may affect the body in one or two ways: (*a*) by the absorption of toxins and bacteria into the blood stream; (*b*) by swallowing pus containing toxins and bacteria.

Riggs and Hunter were early pioneers in establishing the relation that diseases of the mouth (oral sepsis) may bear to many systemic conditions. Arthritis, fibrositis, acute and chronic forms of endocarditis, myocarditis, nephritis, neuritis, sciatica, peptic ulcer, pernicious anemia, diseases of the eye, certain forms of headache and various disturbances of the nervous system, considered functional in origin, have been initiated by oral sepsis.

Oral sepsis may remain local for a considerable period of time before producing systemic manifestations. Prolonged convalescence from illness or surgical operations may offer favorable conditions for foci of infection to become evident. Infection in other parts of the body may aid an oral infection to produce systemic disease. This fact is of importance because the physician not infrequently is disappointed, after having removed the oral infection, in not having relieved the metastatic symptoms. It emphasizes the necessity of a diligent search for other possible foci of infection. The relation that infection in the mouth may bear to diseased conditions elsewhere, as in the gall-bladder or appendix, has been established.

Many individuals harbor foci of infection, and it is the rule rather than the exception to find individuals of mature years with foci of infection, especially of the mouth. These infections are without doubt among the important factors in the production of the degenerative diseases of later life.

The swallowing of pus in dental cario-necrosis, in alveolar infection, gingivitis and in stomatitis leads to disturbances of the gastro-intestinal, biliary, and pancreatic systems.

DIAGNOSTIC DIFFICULTIES IN ESTABLISHING THE EXACT FOCUS RESPONSIBLE FOR INFECTIONS

Many physicians were slow to grasp the truth about the deleterious effects and the relation that foci of infection in the mouth bear to systemic diseases. Many investigate the subject with a total lack of discrimination. The result is that many patients have their illness attributed to infected teeth and tonsils upon insufficient study. Unquestionably many teeth are extracted without proper reasons. On the other hand, many infected teeth are left, which, if the patient is to improve or be cured, must be removed. These errors result in the discredit of a sound principle. The lesson is that before it is definitely decided that the teeth are the cause of systemic disturbances, a very thorough and comprehensive study should be made of other possibilities.

Dental Sepsis.—It is acknowledged that this plays a very important role in focal infection, more so with increasing age. The principal difficulty is to determine what part dental sepsis plays, what kinds of dental sepsis are detrimental by metastasis, and what sorts are of purely dental interest. These points are much in dispute. Dental sepsis ordinarily includes excessive tartar accumulation on teeth, pyorrhœa alveolaris, dental caries, periodontitis, apical infection, and infection around an unerupted tooth or a buried root.

Teeth may look badly because they are covered with an accumulation of tartar. If this tartar has not produced an inflammation of the gums so that infection has spread down into the gums along the teeth, no great harm is done. Allowed to continue, tartar deposits on teeth usually end in a real dental sepsis. Dental sepsis does not necessarily begin with tartar deposit but this should be properly treated and its formation thereafter prevented if possible.

Caries of the teeth may be a source of focal infection by absorption into the blood stream through the carious area. Pyorrhœa alveolaris is an inflammation around the tooth which results in the formation of pus in the linear spaces around it. On pressing the gum at the side of the tooth a drop of pus is squeezed out and becomes visible at the neck of the tooth. As this process continues and periodontal absorption takes place the teeth no longer have support and are easily removed or drop out. The greatest danger in pyorrhœa exists in its early stages when the pus is impeded in its escape around the tooth, with the resulting absorption. Later, deleterious effects may result from swallowing the pus and the organisms in it.

A general catarrhal condition of the mouth and a characteristic fetor are usually present. The disease may persist for months or years and while it lasts there is constant swallowing of the purulent exudate, which in time may cause local disturbances in the stomach in addition to general disease. The part played by these factors in the production of digestive disorders is often overlooked. The diagnosis of this condition is readily made, as a rule several or more teeth are affected. The swollen, receding gums and the oozing of pus from pockets beneath the margin are easily seen. Early recognition of pyorrhœa and prompt and efficient treatment by a dentist are most important.

"Apical infection" is shown in the roentgen-ray film as a dark area at the apex of the tooth, and may be unsuspected except when discovered by the skiagram. Apical infection is almost exclusively present in "crowned teeth" and carious teeth, which have or have not been filled. Apical infection is of infinitely greater moment than pyorrhœa. Although this condition is frequently referred to as an apical abscess there is usually no pus present but a curious jelly-like substance taking the place of the absorbed bone. This jelly-like substance is nearly always infected and toxin can only escape into the lymphatics or the blood stream, unless it develops into a "gumboil." Apical abscesses are dangerous foci of infection and demand removal either by extraction of the tooth or amputation of the root and thorough drainage of the area.

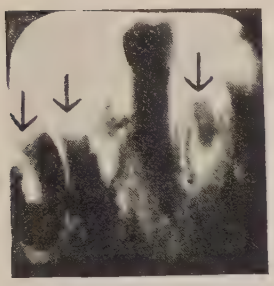
Some authorities, even in the absence of radiographic evidence, believe that a very large percentage of devitalized teeth are infected and therefore potential sources of focal infection. This conclusion seems radical, but time and future studies will determine how correct it is.

Unerupted teeth and buried roots of teeth may be imbedded in an area of infection from which toxins may pass into the blood stream. These conditions are only discovered by roentgen-ray examination. In searching for foci of infection in individuals having no visible teeth and who have disease in other parts of the body, a roentgen-ray examination of the jaws should always be made to rule out the possibility of unerupted teeth or buried roots. Some instances of remarkable relief and cures of diseased conditions of the body have followed the discovery of such sources of focal infection and their prompt removal.

Treatment.—The advice and coöperation of a competent dentist in matters of oral sepsis are needed. Prophylaxis and early recognition are important. All salivary deposits must be removed and the surfaces of the teeth should be scaled and polished. The mouth should be frequently cleansed with a mouth wash, such as liquor antisepticus or an aqueous solution of phenol (1 per cent.) Chlorine water, sufficiently diluted with water so as not to irritate the inflamed mucosa is an excellent mouth wash. A 1 to 1500 solution of permanganate of potash is an efficient mouth wash, especially if considerable fetor is present. As a stimulating application to the gums after mechanical cleansing either tincture of iodine or glycerite of tannin may be used. The use of autogenous vaccines with proper local treatment gives excellent results in some cases.

Offensive Breath. The unfortunate possessor of an offensive breath (halitosis) is seldom directly aware of it. Among the causes are lack of

Fig. 21



Infected buried stumps of teeth.

Fig. 22

Unerupted impacted lower molar tooth.

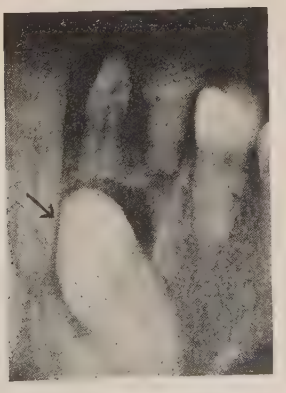
Fig. 23

Periodontal rarefaction.

Fig. 24

Apical abscess.

Fig. 25



Unerupted tooth.

care of the mouth; mouth breathing due to the existence of adenoids, enlarged tonsils, or badly placed teeth; poorly fitting artificial devices; ozena, empyema of the antrum, tonsillitis, diphtheria (in the last the odor is characteristic); local diseases of the mouth, as the various forms of stomatitis, especially the mercurial form; scurvy and caries of the teeth. In most acute febrile diseases the breath is somewhat offensive; in typhoid fever it is quite peculiar. A rather characteristic offensive breath is found in cirrhosis of the liver (Rolleston). It resembles the smell of dried and decomposing blood. It is probably due to a failure of the antitoxic function of the liver.

A *sweetish* breath is common in chlorosis and in diabetes; the odor is fruity in diabetes with acid intoxication, also in the non-diabetic forms of acidosis; a urinous odor is found in uremia; and a peculiar odor difficult to describe characterizes septicemia. A permanent offensive breath is found in diverticulum of the œsophagus and in certain cases of atony and dilatation of the stomach. The odor in the latter cases is probably disseminated by the expiratory air, the gases producing it being taken up by the blood and eliminated through the lungs. This is also true of some cases of cystitis with ammoniacal decomposition of the urine. An offensive breath is common in carcinoma of the larynx, in some forms of bronchitis, in pulmonary tuberculosis when there are cavities, and in abscess and gangrene of the lung. A particularly repulsive fetor is sometimes due to putrid plugs in the crypts of the tonsils. In hemoptysis the breath has a somewhat sour odor. There is sometimes an offensive breath in menstrual disorders and after the use of certain drugs, as arsenic, phosphorus, the bromides and iodides. The offensive odor following the abuse of alcohol is more often due to fusel oil and other ingredients than to the alcohol itself.

Treatment.—Most important is the determination of the cause and its removal, if possible. In addition, the use of antiseptic mouth washes is indicated. Miller recommends the following:

℞—Acidi benzoici	gr. xc	(6.0)
Ol. menthæ pip.	♏xv	(1.0)
Tr. eucalypti	ʒj	(30.0)
Alcohol. absol.	ʒiij	(100.0)

A very satisfactory wash is the liquor antisepticus of the Pharmacopœia; also the following:

℞—Potass. chloratis	5.0
Tr. myrrhæ	5.0
Aquæ rosæ q.s. ad.	90.0

DISTURBANCES OF SENSATION

A. **Disturbance of General Sensation.**—(*a*) **Anesthesia.**—This is usually of hysterical origin, and more often unilateral than bilateral. As a rule, it extends to all qualities of sensation. In the rare cases not due to hysteria, the lesion involves the superior or inferior maxillary nerve or the tympanic plexus, or is located in the cerebrum, in which case there is complete anesthesia of one-half of the body.

(*b*) **Hyperesthesia and paresthesia** (formication, pricking, tingling) are usually the accompaniment of local processes, as the various forms of stomatitis; but they may be due to hysteria or to lesions of the central nervous system. They may, especially paresthesia, be the precursors of anesthesia and paralysis.

B. **Disturbances of Taste.**—Abolition of taste, *agusia*, may be general or partial, persistent or transitory. Transitory agusia depends on local conditions, being common in dryness of the mouth, particularly when that is due to oral breathing. If partial, it may affect one-half of the tongue or the anterior or posterior portion. In agusia of the anterior third the lingual nerve or the chorda tympani is involved. In glossopharyngeal lesions the agusia affects the posterior portion of the tongue. Centric agusia, that is, agusia due to disturbances in the gustatory centre in the uncinate gyrus, is theoretically conceivable, but has not yet been demonstrated. Agusia may coincide with general anesthesia of the mucous membrane, such as is found in hysteria. Hyperagusia is practically seen only in hysteria.

Paragusia, or gustatory paresthesia, is common in hysterical persons and in the insane. It is also observed in some cases of facial palsy and in old cases of otorrhœa; in both of these it affects the half of the tongue on the diseased side. Sometimes the epileptic aura takes the form of an abnormal gustatory sensation. In persons with fever and in those suffering from gastric disturbances there is at times a total perversion of taste, on account of which tastes agreeable to them in health become insupportable. The senior writer had under observation a man suffering from neurasthenia and moderate arteriosclerosis, who had constantly a sweet taste, for which no cause could be found. There was no diabetes and no abnormality in the mouth to explain it.

In the absence of febrile affections and peripheral nerve lesions, the prognosis in paragusia should be extremely guarded, as it may be a forerunner of mental trouble.

THE LIPS

In a state of health the border of the lips is of a bright red color, which disappears on pressure, but returns instantly. There are marked differences in thickness and in the amount of mucous membrane exposed. A thick lower lip is characteristic of certain races, and is seen pathologically in myxœdematous idiots. The upper lip is thickened in the scrofulous.

The so-called *double lip* is a hypertrophy or enlargement not of the whole lip, but of the labial glands, which causes a projection between the teeth and the red portion of the lip. The appearance produced is as if the affected lip were doubled, hence the names "lèvre double" and "Doppellippe." According to Eddington,[1] it occurs in young men, and affects especially the upper lip. The writer has also seen it in a woman. A lip thus deformed is liable to become dry, cracked and ulcerated.

[1] *Glasgow Med. Jour.*, 1906, **65**, 81.

The treatment consists in the removal of a strip of mucous membrane, including all the enlarged glands.

A change in the *shape* of the lips may occur as the result of long-continued mouth breathing. The lips are pale and flabby, the upper lip is shortened, the lower often thick and rolled outward.

Fissure of the lips is common, and occurs usually in the centre, but also at the angles. Fissures at the angles of the mouth, rhagades, are most frequently seen in congenital syphilis and in scrofula.

Changes in the *color* of the lips and of the mucous membrane of the mouth are common. The lips are blue or cyanotic on exposure to cold, in asphyxia, in pneumonia, in emphysema, in congenital and in some types of acquired heart disease, in mediastinal tumor, in rupture of an aneurism into the superior vena cava, in polycythemia rubra and in poisoning with coal-tar products. In one of the writer's patients an attack of enterocolitis was always preceded and accompanied by intense blueness of the lips. Pallor of the lips and oral mucous membrane is found in anemia, hemorrhage, chronic parenchymatous nephritis, and in aortic stenosis. It is not always a positive sign of anemia, as the blood may be fairly normal and yet the lips be pale. In conditions leading to inspissation of the blood, as in carcinoma of the alimentary tract, the lips may be of a deep red, almost maroon color. In diabetes there is at times a striking redness of the lips, which the writer has usually found associated with a similar condition of the ears. In jaundice the mucosa on the inner surface of the lips has a yellowish tinge, which becomes more noticeable if the blood is pressed out with a glass slide. Semmola and Geoffreddi[1] state that if a jaundiced patient forces his mouth wide open, two yellow streaks can be seen on the soft and a portion of the hard palate. In lead poisoning, in addition to the characteristic blue line along the gums, there may be flame-shaped, bluish patches on the inside of the lips. In the so-called blue-gummed negro, bluish or brownish pigment stains are seen on the gums, rarely on the inside of the lips. The presence of brownish patches on the inside of the cheeks, on the palate, or lips is an important diagnostic sign in Addison's disease.

Unnatural *dryness* of the lips occurs in fevers and in ordinary colds. In the former the lips and teeth are often covered with brownish crusts called sordes, which when picked leave a bleeding surface. *Tremor* of the lip is seen in general paresis, in alcoholism, in hysteria, and in typhoid and other long-continued fevers.

Eruptions.—The most frequent is the fever blisters—*herpes labialis*, cold sore—usually found on the skin surface and red border. There may be but a single vesicle, more often there are several, which become confluent with the formation of reddish-brown crusts. Herpes simplex is most common in childhood and early life. Herpes is an accompaniment of ordinary colds, pneumonia, malaria, and cerebrospinal meningitis. It is comparatively rare in influenza, and exceedingly uncommon in typhoid fever. There is a belief among clinicians that the occurrence of herpes in pneumonia is a favorable omen.

[1] *Twentieth Century Practice*, 1897, **9**, 477.

PLATE I

The Blue Line of Lead Poisoning, with a Deposit of Lead in the Lower Lip.

Herpes is of infectious origin; but the cause is probably not a single specific microörganism.

Treatment.—Spirit of camphor freely applied in the earliest stages may abort an outbreak of herpes; the lesions when present may be painted over with tincture of benzoin—several applications are made and allowed to dry; they are repeated two or three times daily. When crusts have formed, ointments, such as cold cream, camphor ice, zinc ointment, etc., favor their early separation.

Eczema is common in the upper lip in children having acrid nasal discharges. Parasitic skin diseases may attack the lips.

Inflammation of the Labial Glands.—Baelz's Disease.[1]—This is a chronic disease affecting the mucous glands of the lips. It begins as an indolent swelling and gradually leads to ulceration, without causing either enlargement of the lymph glands or constitutional symptoms. It probably depends on a special infection, but is not syphilitic, although its appearance may lead to the suspicion that the patient has a labial chancre. There is usually an accompanying superficial catarrhal stomatitis. The disease yields readily to applications of dilute tincture of iodine.

Tumors of the Lips.—The principal tumors of the lips are angioma (hemangioma), lymphangioma, and carcinoma.

Harelip.—This is a congenital deformity, consisting of one or more fissures in the upper lip, resulting from an arrest of development. The fissure is not in the median line, but corresponds to the line of junction between the intermaxillary and superior maxillary bones. Harelip may be single or double. The treatment is surgical.

THE MOUTH

INFLAMMATION OF THE MOUTH

Catarrhal Stomatitis.—Catarrhal, simple, or acute stomatitis is a mild disease, characterized by redness and swelling of the mucous membrane and by increased secretion of saliva. It is produced by irritants acting not too violently, these being mechanical, thermic, or chemical; as food too hot, too cold, too highly seasoned, or too sour; alcohol, tobacco; sharp edges of decayed teeth, caries of the teeth, tartar, dentition, difficult or fruitless sucking, hare-lip, the use of pacifiers, etc., improper care of the mouth, badly fitting teeth, and mouth breathing. Catarrhal stomatitis is present in many infectious diseases, partly as a result of the same cause, partly because of decomposition of food in the mouth, etc. Thus it is found in scarlet fever, measles, typhoid fever, influenza, smallpox, and gastric and intestinal disorders. It is also present, either alone or as an accompaniment of other forms of stomatitis, after the use of certain drugs, such as mercury, iodides, lead, bromides, bismuth, and arsenic. Guy[2] and Bunten[3] report severe cases of stoma-

[1] Unna, *Monats. f. prakt. Dermat.*, 1890, **11**, 317.
[2] *Jour. Am. Med. Assn.*, 1924, **82**, 2119.
[3] Ibid., 1443.

titis as a result of using mercurochrome. In diabetes, nephritis, and cachectic states a more or less pronounced catarrhal stomatitis is often found. When the process is confined to the gums it is designated gingivitis.

Pathology.—Hyperemia, increased secretion, and proliferation of cells are the changes usually found. The ordinary mouth bacteria are present in augmented numbers.

Symptoms.—There is moderate pain, which is increased on the ingestion and mastication of food; infants and young children are apt to cry and to protrude the tongue; sucking is difficult. The saliva is increased in quantity and becomes sticky and pasty. The sense of taste is impaired; the appetite diminishes; and in children there may be fever and at times even emaciation. Examination reveals swelling and redness of the mucosa; the tongue is tooth-marked; the interdental processes of the gums are enlarged, red, and thickened. The mucosa is covered with a tough, whitish saliva, usually in patches. In severe cases the papillæ of the tongue are prominent and bloody at their tips (papillitis). The breath is offensive.

Treatment.—Aside from the removal of the cause, cleanliness is usually all that is required. Simple antiseptic mouth washes, such as a 2 to 3 per cent. solution of boric acid, sodium borate (2 to 3 per cent.), or potassium chlorate (1 to 3 per cent.) will suffice. If the gums are spongy they may be touched with glycerite of tannin (1 to 10), and a little tincture of myrrh may be added to the mouth wash. In infants, the mouth, after nursing, should be washed with sterile water and the antiseptic then applied on a pledget of cotton or linen.

Aphthous Stomatitis (*Mucofibrinous Stomatitis*).—This is characterized by the formation of cream-white patches or plaques firmly adherent to and embedded in the mucosa. It is most common in children, but may occur in adults, especially in women at the menstrual periods, after parturition, and during lactation. It is rare before dentition, and increases in frequency with its beginning and up to the end of the second year. There is in some cases a marked tendency to recurrence.

Etiology.—There is a wide divergence of opinion regarding the nature of this disease. Some observers have described staphylococci as being the chief organisms found in the aptha, while others have found short chain streptococci. It is evident that the organisms found are by no means constant, and no conclusive evidence is at hand in the nature of inoculation experiments. Faulty hygiene of the mouth, decomposition of food remnants and the irritative influences of dentition are predisposing factors. The disease is infectious.

Symptoms.—Aphthæ are small, round, or oval plaques or ulcers varying in size from that of a pinhead to 0.5 cm. in diameter. They form with great rapidity, are sharply circumscribed, and surrounded by a reddish, slightly elevated border. The favorite sites are the tip and edges and under surface of the tongue, the inside of the lips, and the labiogingival pouch. Their number is usually small, although at times new ones appear as the old ones undergo healing. Often two ulcers are located opposite each other on the gums and on the lip. The pain is usually

intense, quite out of proportion to the importance of the affection, and interferes with mastication. Salivation is present, the tongue is coated, the breath offensive, the temper irritable; there may be a little fever. Reference has been made to recurrent aphthæ; in persons predisposed to them any trivial disorder of the general health may bring on an attack of aphthous stomatitis. Aphthæ do not lead to scar formation.

Treatment.—The digestive tract and general health must receive attention, only in this way can the tendency to recurrence be removed. The local treatment consists in the use of antiseptic washes and, if necessary, mechanical cleansing of the teeth by a dentist. The ulcers may be touched with caustic, preferably the solid stick of silver nitrate. Baginsky recommends the application of a solution of potassium permanganate (1 to 150). Hirsch advises tincture of iodine or a 10 per cent. solution of chromic acid. Alum is also useful.

A *confluent form* of aphthæ in children is described by du Pasquier.[1] It is a serious affection, and is either primary or secondary to bronchopneumonia, gastro-intestinal disorders, or one of the exanthems. The lesions may appear benign at first, but are rebellious to treatment. There is fever and emaciation; at times an infectious erythema appears and constitutes a grave symptom. The disease lasts from one to two weeks, and may terminate in bronchopneumonia or meningitis. There is also a fulminant form ending fatally in twenty-four or forty-eight hours after the appearance of the aphthæ. The most striking post-mortem finding is a fatty degeneration of the liver.

Bacteriological examination of the oral lesions shows a polymicrobism, various round and rod-shaped organisms and Vincent's spirilla being found. It is quite probable that this form of stomatitis and the ordinary aphthous form are two etiologically different diseases. An affection resembling aphthæ, but at times forming more diffuse whitish patches has been described by Mann[2] and by Schomerus.[3] In the lesions the pneumococcus was isolated in pure culture.

Ulcerative Stomatitis.—The term ulcerative stomatitis is loosely used to designate ulcerative conditions in general as well as a specific disease of indeterminate etiology. It occurs in children and adults, and is largely due to lack of care of the mouth, decayed and sharp-edged teeth, and in children to improper feeding. Crowding of the teeth is also an important factor, ulcers not rarely forming on the cheeks and gums from pressure by wisdom teeth. Poisoning with mercury, lead, phosphorus, and iodine is a predisposing cause, as are also infectious diseases, scurvy, etc. Older writers have described epidemic outbreaks of ulcerative stomatitis, especially in barracks; but the condition was probably a different one, in some cases perhaps foot and mouth disease.

Bacteriology.—In addition to the common pyogenic organisms, the fusiform bacillus of Vincent (Plaut-Vincent) is probably an important factor in the production of the disease. This bacillus is a polymorphic anaërobe, growing at 37° C., on serum-containing media. It is practically always associated with spirochetes, and is found in a great variety of

[1] *Rev. mens. d. mal. de l'ebf.*, 1903, **21**, 353.
[2] *Münch. med. Wchnschr.*, 1909, **56**, 72.
[3] *Ibid.*, 1909, No. 4.

affections, *e. g.*, ulceromembranous angina, hospital gangrene, tropical ulcer, mercurial stomatitis, scurvy, pulmonary gangrene, peribuccal abscesses, and noma. Both the bacillus and the spirochete stain easily with dilute carbol fuchsin. The latter has been cultivated by Mühlens.

Symptoms.—The process, which is almost invariably limited to the region of the teeth, begins at the margin of the gums. The gums swell, become dull red in color, and are covered with a veil-like haziness; subsequently they become yellowish and necrotic, bleed easily, and stand away from the teeth. In the early stages the swollen gums may in part envelop the teeth, while the interdental processes protrude as thick, red ridges. As the edges ulcerate the teeth become more and more exposed. By lifting away the gums from the teeth, ulcers may sometimes be discovered quite early on the dental surface below the free edge. The ulcerative process may spread to contiguous parts of the lips, cheeks, or tongue, and the teeth may drop out. Salivation is profuse, and the odor of the breath horribly fetid. Chewing and swallowing are difficult, and in children there is fever; even in adults there may be slight rises of temperature. The duration varies from a few days to several weeks, but as a rule is not more than ten days.

Treatment.—Removal of the cause is of prime importance. The teeth should have careful attention and the mouth should be cleansed with antiseptic washes, such as the liquor antisepticus or hydrogen peroxide. Internally potassium chlorate in small doses seems to be of much value, but it should be administered with caution, especially in children; its use should not be prolonged. In severe cases the employment of silver nitrate locally is helpful. Arsphenamine has proved useful in Vincent's angina. This would justify its employment in severe cases of ulcerative stomatitis due to the Vincent bacillus and spirochetes.

A few words may be devoted to *mercurial stomatitis* (salivation), a subvariety of the ulcerative form. Its mode of origin is not quite clear, but it is generally held that the mercury, by its reducing action, injures the tissues and in that way prepares the way for pathogenic bacteria. Some persons have an idiosyncrasy to mercury, and in them a single small dose, or perhaps two or three small doses, will produce salivation. Preëxisting diseases, such as chronic nephritis, cirrhosis of the liver, etc., favor its development. Infants without teeth and the edentate aged are not liable to mercurial stomatitis. In grave cases death may ensue from extensive ulceration or gangrene and septic absorption.

The *treatment* consists in the discontinuance of the mercury and the use of antiseptic washes, as hydrogen dioxide (2 to 3 per cent.), and, internally, potassium chlorate, gr. ij to iv (gm. 0.12 to 0.24). The application of potassium chlorate in powder or in the form of a 50 per cent. tooth paste is useful.

Gangrenous Stomatitis.—*Synonyms:* Noma; cancrum oris; Wasserkrebs (German). This is a comparatively rare form of infection of the mouth. Like hospital gangrene, which in some respects it resembles, it was more frequent in preantiseptic days. Its chief feature is a rapidly spreading gangrene involving the cheeks, gums, and alveolar processes. It is more common in childhood and in hospital than in private practice.

Although occasionally an independent affection, it is, in the majority of instances, an accompaniment of or sequel to infectious diseases, such as measles, scarlet fever, diphtheria, typhoid fever, whooping-cough and dysentery. In rare cases it follows mercurial stomatitis. The old view that it is caused by the administration of mercury has been disproved. It usually affects children between the ages of two and five years, and seems to be more common in the spring and autumn; in adults it is exceedingly rare. Some authors have reported cases of so-called idiopathic gangrene of the mouth, in which the disease set in spontaneously without any preceding illness.

Bacteriology.—Various bacteria have been isolated in culture or found in stained preparations, but the crucial test of reproducing the disease by inoculation has not been done. The most common organisms are the fusiform bacillus and the spirillum of Vincent. Streptococci, staphylococci, pseudodiphtheria bacilli, and perhaps true diphtheria bacilli and pneumococci are also found. Hellesen[1] isolated a Gram-positive, non-encapsulated diplococcus, which in animals produced a typical and specific necrosis of tissue.

Symptoms.—The cheek and lip become swollen and the overlying skin glazed, colorless, and hypesthetic; a small ulcer forms on the mucous surface, rapidly becomes gangrenous, and advances in depth and width until the integument is reached. If the latter also melts down in the gangrenous process, a perforation results. The hole may be small, or the gangrene may speedily involve nearly the entire cheek, the gums, and even the alveolar processes, so that the teeth are exposed and loosened. In the gravest cases, the tongue and palate may become affected. In rare instances, the gangrene involves the outer parts of the cheek and spares the mucosa. Noma is nearly always unilateral.

The constitutional symptoms are often strangely mild when contrasted with the local process. Fever may be present; when present it is usually of a hectic character, at least in the terminal stages. The odor is very foul; the submaxillary lymph glands are enlarged. The disease has a very high mortality—from 75 to 80 per cent. The duration is from one to two weeks; recurrences have been noted. Death is due to bronchopneumonia or toxemia, in some cases hastened by a septic diarrhœa.

Treatment.—Removal of the diseased tissue by the knife or Paquelin cautery under anesthesia, the wound being afterward dressed antiseptically, is the most efficient treatment. Destruction of the odor is best accomplished with formaldehyde, potassium permanganate, or iodoform. Diphtheria antitoxin has been employed in some cases, on the ground that the diphtheria bacillus was present; but it is quite probable that the organism was the pseudodiphtheria bacillus. An abundance of nourishment should be given.

Swoboda[2] described a gangrenous inflammation of the *tooth germ* in the new-born, causing a destruction of the gums, with subsequent sequestration of the crowns of the teeth in infants that are still far from the normal period of dentition. The cause is probably a septic infection, and the prognosis is always fatal.

[1] *Jahrb. f. Kinderh.*, 1908, **67**, 294.

[2] *Die Therapie der Gegenwart*, 1904, **45**, 515.

Thrush.—*Synonyms:* Mycotic or hyphomycetic stomatitis; soor (German); muguet (French). Thrush is a form of stomatitis characterized by the formation of whitish patches largely composed of the causative fungus, the *Oïdium albicans*. It occurs chiefly in infants, rarely in adults.

The *Oïdium albicans* is generally accepted as the etiological agent; although some authorities hold the *Saccharomyces albicans buccalis* to be the cause. The oïdium is a pleomorphic organism presenting under two forms, (*a*) small, yeast-like bodies and (*b*) filaments, both of which are usually found together in the mouth. The virulence of the organism may be augmented by passage through animals. Although in the body the oïdium probably elaborates a poison, none has been found in artificial cultures.

Rajat and Péju[1] have isolated two types of fungus, one in which the cells are of the average size of yeast cells and the other in which they are from six to eight times as large. The small-celled variety was present in all (70) the benign cases, that is, in those yielding promptly to treatment; the large-celled forms were present in 5 tenacious cases.

Thrush seldom, if ever, appears in healthy individuals; but chiefly in those whose vitality is impaired. In infancy trivial disorders may prepare the way—simple colds, slight intestinal disturbances; while in older children and adults, usually the aged, pneumonia, typhoid fever, and the exanthemata are the predisposing causes. An acid condition of the saliva, normal in infants and in older children easily produced by fermentation of milk remnants, facilitates the growth of the fungus. The too vigorous washing of the mouth practised by some nurses after the birth of the child may act in the same way. The disease is infectious and is transmitted by dirty nipples and dirty feeding bottles.

Symptoms.—The first sign is the formation of small, whitish points on the tip and edge of the tongue and on the inner surface of the lips, places on which desquamation of the mucous membrane is favored by the act of sucking. The points grow into patches of varying size, and may cover the entire inner surface of the mouth like a coat of plaster. In some cases the disease extends to the œsophagus and stomach; the nose and larynx may also be affected, rarely even the vulva. The patches consist of mycelial threads and epithelial cells, with leukocytes in small numbers. The mucosa is red and bleeds easily if the patches are forcibly detached. Nursing in infants and in older children deglutition and mastication are difficult. There may be slight fever and restlessness; an eczema of the buttocks is sometimes noted. Several writers have recorded cases of thrush metastasis.

Diagnosis.—All that is necessary is to examine a bit of the deposit under the microscope. Sometimes the patches are mistaken for curds of milk, which in appearance they closely resemble.

Treatment.—For prevention, pasteurization of the milk and cleansing of the bottles and of the mouth after feeding are important. Ordinarily, the disease yields readily to simple measures, such as wiping away the patches with a piece of soft linen or gauze soaked in boric acid or sodium

[1] *Comp, Rend. Soc. de Biologie.*, 1906, **61**, 523.

PLATE II

FIG. 1

FIG. 2

Herpetic Inflammation of the Mouth and Tongue

PLATE III

Herpetic Inflammation of the Mouth and Tongue.

bicarbonate solution, the mucous membrane being afterward brushed with the same solution, or with a weak solution of mercuric chloride (1 to 4000), sodium hyposulphite (1 to 25), or a weak solution of borax or potassium permanganate. Such constitutional treatment as is suggested by the underlying conditions must be instituted.

Herpetic Stomatitis; Herpes Buccalis; Stomatopharyngitis Herpetica or Herpetiformis.—Various herpetiform eruptions affect the mouth aside from the simple herpes of the lips. Some are associated with herpes of the pharynx; others are limited to the oral cavity, usually its posterior portion. In a case of the writer's, the vesicular eruption involved the tongue, lips, gums, and tonsils, and it was associated with a violent conjunctivitis. (See Plate III.) The vesicles were small, yellowish white, and on the gums became confluent. There was some fever, inability to swallow, salivation, and pain. The condition presented the picture of an acute infection. Only one culture was made, and that was negative. As pneumonia is an occasional, though rare, complication of herpes of the mouth and pharynx, the latter may, like the former, be of pneumococcic origin. In women a herpetic stomatitis sometimes occurs at the menstrual period.

Treatment.—This consists in the use of the milder antiseptic washes, as, for example, liquor antisepticus (1 part to 2 or 3 parts of water).

Gonorrhœal Stomatitis.—This occurs in the newborn from five to twelve days after birth, in the form of whitish patches on the anterior two-thirds of the tongue, leaving a free border from 2 to 5 mm. wide: also on the anterior half arches, and the posterior border of the alveolar process of the upper jaw, along the free edge of the gums anteriorly, and occasionally on the frenum of the tongue and lips. A reddish reaction zone surrounds the exudate. The functional disturbances are slight, and the process heals without scars in from four days to four weeks. In adults it is rare. The cause in children is infection of the mouth with the gonococcus during birth.

Treatment.—Silver salts in dilute solution (1 to 2 per cent.), as a rule, bring about rapid cure; mercuric chloride (1 to 7000) may also be used.

Bednar's Aphthæ.—These are small, whitish plaques occurring in the newborn in the region of the hard palate. They are probably due to pressure of the tongue or the nipple during sucking, their development being favored by the general tendency to epithelial desquamation in the first few days of life. Forcible cleansing of the mouth, practised after birth by some nurses, may be the real factor. The ulcers heal spontaneously as a rule; in rare cases they constitute the atrium of a general infection.

Torus Palatinus.—This is a congenital anomaly and consists of a bony protrusion in the mid-line of the hard palate. It is usually present at birth, but may develop later. It occurs more frequently in females than males and does not cause symptoms. The diagnosis is made by inspection. Various observers, without sufficient evidence, have regarded this condition as a sign of tuberculosis, syphilis, degeneracy and pulmonary osteoarthropathy.

TUMORS OF THE MOUTH

Carcinoma. This may start in the mucous membrane of the cheeks, the gums, about the angles of the mouth, the lips, or in the floor of the mouth. It is usually of the squamous type, more frequent in men than in women, and very malignant. Early operation is the only treatment that promises good results.

Cysts. The most common cystic tumor of the mouth is the so-called ranula (French grenouillette), which may arise from the sublingual gland or its ducts, from Wharton's duct, or from a small group of glands the glandula incisiva in close proximity to the neck of the middle or lateral incisor. In rare instances a ranular growth may take its origin from the remains of the thyroglossal duct, or from the branchial clefts, or finally, from Blaudin-Nuhn's glands on the under surface of the tongue. It is at times difficult in a given case to determine the origin of a cyst, but it may be remembered that those from the thyroglossal duct have a lining of columnar ciliated epithelium, while those arising from the acini or excretory ducts of the salivary glands have a lining that more or less faithfully reproduces the epithelium of the parent structure.

Suprahyoid and submental cysts are sometimes found associated with cysts of the sublingual region, with which they may communicate, but they may also exist independently. The ordinary ranula results from obstruction of the gland duct, and is in its nature a chronic tumor. An acute ranula has also been described; it is due to an acute inflammation of the duct of the submaxillary or sublingual gland, or of both. Cysts of the parotid gland are extremely rare. One with a lining like that of the mouth is reported by Morestin.

Symptoms. The characteristic symptom of ranula is the presence of a cystic tumor on the floor of the mouth, usually just to one side of the median line, pushing up the mucosa, which is tightly stretched over it, and displacing other structures. Fluctation is easily obtained.

Treatment. Evacuation of the contents is an uncertain method, unless combined with strong cauterization of the lining wall. In some cases excision is necessary.

A *dermoid cyst* on the floor of the mouth has been described by Brentano.[1] Choisser[2] reported a *sarcoma* in the soft palate of a child, aged twenty-three days. *Mixed tumors* are also found in various parts of the mouth.

DERMATOSES OF THE MOUTH

Various affections of the skin may simultaneously or independently affect the mucous membrane of the mouth.[3]

Urticaria. In severe cases of urticaria, especially in giant urticaria, similar lesions may appear in the mouth. The tongue and uvula may

[1] *Deut. Med. Wchnschr.*, 1906, p. 164.

[2] *U. S. Naval Bull.*, Washington, 1924, **20**, 451.

[3] Only the most important can be mentioned here; for a fuller account the reader is referred to text-books on diseases of the skin, particularly to Stelwagon, Schamberg, and especially the exhaustive work of Trautmann.

be enormously enlarged; there is intense burning and thirst and at times alarming shortness of breath.

Angioneurotic œdema is characterized by a sudden painless swelling of the parts involved. The lips when affected, and they are a very common seat of the disease, are swollen to an enormous size and stand out as huge, stiff, fleshy masses. It is most common in women, and has a tendency to recur. Gastro-intestinal symptoms, especially nausea and vomiting, may be present, but are not constant.

Treatment.—The œdema tends to disappear spontaneously, and remedies seem to have but little influence over it. Benefit may be gained from calcium lactate, given in 10 grain doses (gm. 0.6) three times a day. If there is any disorder of the gastro-intestinal tract, this must be corrected, and the diet should be simple.

Psoriasis.—It is doubted by many whether psoriasis occurs on the mucous membrane. In the cases in which no lesions of the skin existed, the buccal disease was either leukoplakia or some other non-psoriatic condition. A probable genuine case is, however, reported by Oppenheim.[1]

Lupus Erythematosus.[2]—This invades the mouth from the face and usually presents itself as superficially inflamed areas, having an elevated, deep-red border marked radially by dilated veins; in the centre of the patches the mucous membrane is atrophic, violaceous, and dotted with countless fine white or bluish-white points or lines. Some of the plaques show erosion of the surface and are covered with a yellowish-white deposit that cannot be detached. In older foci the appearances may be somewhat different—the edges are less elevated, and usually have extending from them fine arborescent prolongations. The most frequent seat of lupus erythematosus is the cheek corresponding to the space between the upper and lower teeth. In the differential diagnosis, eczema, lichen planus, pemphigus, leukoplakia, and perhaps psoriasis have to be considered.

Treatment.—This consists in counterirritant and absorptive applications and cauterization, but is usually of little avail. Lupus erythematosus is not greatly influenced by the roentgen-rays.

Lichen Planus.—The lesions of the mouth are nearly always found in association with lichen planus of the skin; in rare instances they antedate the latter. They appear in the form of whitish dots, plaques, or streaks, giving to the mucous membrane an appearance as if it had been cauterized with silver nitrate. The lesions are unattended by any inflammatory reaction and may persist for years without change. The disease is most common in those whose nervous systems are depressed.

Treatment.—This in the main is general, the common tonics—iron, strychnine and cod-liver oil—being indicated. Arsenic in ascending doses (up to 10 minims of Fowler's solution) is valuable; mercury is also useful, especially if arsenic fails. Radium is worthy of a trial.

Pemphigus.—Pemphigus may appear on the mucous membrane of the mouth, the lesions being widely scattered over the gums, the roof

[1] *Monat. f. prakt. Dermat.*, 1903, **37**, p. 489.
[2] See the article of Kren, *Arch. f. Derm. u. Syphilis*, 1907, 83, 13.

of the mouth, and the soft palate. Farlow[1] reported two obstinate cases, in which successive crops of vesicles appeared. At various times lesions were also present on the cornea, in the nose, in the vagina, and on the leg. The *treatment* consists in the use of alkaline antiseptic washes to prevent secondary infection, and the administration of arsenic. Local anesthesia (cocaine) may be necessary to render eating possible.

Acne.—This is rarely found on the mucous membranes. Unna[2] described a case affecting the upper lip, in a woman who had acne of the mouth and chin. The lesions yielded to treatment with resorcin ointment and ichthyol soap.

Eczema.—Eczema sometimes affects the vermilion of the lips.

Tinea Circinata.—This may spread from the face to the lips and mouth.

Scleroderma.—This sometimes attacks the mouth, leading to atrophy of the mucous membrane and to its adhesion to the submucous tissue. It may also cause falling out of the teeth.

Erysipelas.—In rare cases erysipelas of the face extends to the mouth, producing a deep redness and swelling of the mucosa, and profuse salivation. The soft palate and uvula are especially involved, and their swelling causes pain and difficulty in deglutition. In severe cases the tongue may be involved, as well as the pharynx and larynx. The diagnosis is only assured if erysipelas co-exists, or has immediately preceded or immediately followed. In persons having repeated attacks of erysipelas, groups of small vesicles are sometimes found in the mouth. They may be of the nature of lymphatic varices.

CHANGES IN THE MOUTH DUE TO GENERAL DISEASE

Typhoid Fever.—In addition to the familiar changes in the tongue, typhoid fever produces alterations in the mouth of a less well-known character. These consist in ulceration, usually on the upper part of the anterior faucial pillar, on the tongue, uvula, cheeks, lips, and labiogingival folds. Devic[3] observed these ulcerations 81 times in 220 cases of typhoid fever (36.8 per cent.). They appear between the seventh and fourteenth days of the disease, are shallow, and are preceded by a slight discoloration of the mucosa. As a rule they heal in from one to two weeks without leaving any permanent defect. Bacteriologically only the common mouth organisms were found in Devic's cases; but the typhoid bacillus is found in some cases. The regions at which the ulcers occur are more or less points of compression. As the ulcers are superficial and heal readily. the maintenance of oral cleanliness is sufficient. The typhoid bacillus may be present apart from ulcers.

Uremia.—The mouth is frequently affected. There may be an insupportable dryness, or an actual stomatitis due to bacterial infection. Instead of dryness of the mouth, there may be salivation without any stomatitis to account for it. Possibly the salivary glands may act vicariously for the kidneys. Uremia may also lead to parotitis. The tongue

[1] *Boston Med. and Surg. Jour.*, 1904, **151**, 671.
[2] *Monats. f. prakt. Dermat.*, 1890, **11**, 321.
[3] Troullieur, *Gaz. des hôp.*, 1908, **18**, 207.

PLATE IV

The Mouth Lesions in Scurvy.

may be dry and of a maroon-red color. In one case of uremia under the writer's care a tough grayish-white membrane covered lips, gums, cheeks, and pharynx—no other organism but the staphylococcus was demonstrable. Salivation was extraordinarily copious.

Diabetes.—The tongue in diabetes is large, red, "beefy," and fissured at the margin; the mouth is dry; the teeth are often carious. Pyorrhœa alveolaris is frequent. Diabetes insipidus presents nothing but dryness of the mouth.

Pernicious Anemia.—In some cases there is marked oral sepsis which Hunter considers an important factor in the etiology. Severe glossitis is not infrequently associated with pernicious anemia. In all cases of "sore tongue" in which syphilis and distinctly local causes can be excluded, the possibility of pernicious anemia must be borne in mind. The tongue is usually small, atrophic, smooth, velvety and may or may not be coated; the color varies. The papillæ are frequently atrophied.

Leukemia.—The mucous membrane of the mouth may become the seat of lymphoid hyperplasia similar to that in the lymphatic glands, spleen, and intestines. The infiltrations show a tendency to undergo necrotic change leading to extensive ulceration and pseudomembranous and gangrenous processes. In acute leukemia, gingivitis and ulcerative stomatitis may be among the first signs. As the gums bleed easily and as there is marked fetor of the breath, the condition may be mistaken for scurvy.

Scurvy.—The gums in scurvy are of a purplish color, soft, and bleed easily; the teeth are loosened; there is salivation and intense fetor of the breath. (See Plate IV.) Babes isolated an organism, *Bacillus gingivitidis,* which is found in association with the streptococcus. Oral changes are not always present in scurvy. In the differential diagnosis the possibility of acute leukemia must be kept in mind.

Foot and Mouth Disease.—This usually occurs in epidemic form. The lesions in the mouth are vesicular, occurring on the lips, tongue and gums, rarely on the pharynx or palate. The vesicles are clear early and later become opaque and rupture, resulting in ulcerations, which may become covered with a whitish exudate. The tongue is swollen and painful. The treatment is largely local. The mouth must be kept clean by the use of a 1 per cent. solution of potassium permanganate; and a 3 per cent. aqueous solution of phenol applied to the ulcer twice daily is useful in promoting healing.

Trench Mouth.—Under this name many cases of Vincent's angina, were classified during the World War. It is probable that various forms of stomatitis were included under this term. The treatment consists of the application locally of a 10 per cent. solution of arsphenamine in glycerin, if it is Vincent's angina; other forms of stomatitis are treated by mouth washes, as described under stomatitis.

Pellagra.—In most cases of pellagra a chronic stomatitis is present.

Sprue.—The mouth is sore and exhibits denudation of the epithelial surfaces of the tongue and oral mucous membrane with areas of painful ulceration. The fungiform papillæ may be seen projecting above the surface of the tongue but the filiform papillæ may entirely disappear.

On account of complete denudation of the tongue the pain produced by taking of food prevents the patient from obtaining proper nourishment and severe wasting results. The gums are pale and ulcerated patches are found more commonly on the inner or buccal surface of the lower lip than on the other parts of the oral mucous membrane. The treatment is local and constitutional. The local treatment of the mouth consists in cleansing with non-irritant lotions as glycerin and borax. The painful areas may be touched with a 2 per cent. solution of cocaine, followed by an application of half strength tincture of iodine. Great harm may be done by the use of escharotics which should not be employed.

Tabes Dorsalis.—Oral conditions found are perforating ulcer (mal perforant buccal) and falling out of the teeth. The latter is usually painless and may be followed by resorption of the alveolar processes. At times there is anesthesia of the mucous membrane. The buccal changes are probably dependent upon a peripheral neuritis.

Pregnancy.—Hyperesthesia, paresthesia, and salivation are common. Sometimes there is inability to chew certain articles of food, which in a case of the writer's extended only to the eating of celery. Pain in the teeth, for the relief of which the teeth are often foolishly sacrificed, is a common symptom. At times there is a true gingivitis.

Varicella.—Lesions may occur in the mouth in chicken-pox, but the vesicular stage is rarely observed.

Variola.—Lesions of the mouth may appear simultaneously with those upon the skin or later; they are in the form of pustules that soon become macerated and transformed into superficial ulcers. The tongue may be spared.

Treatment.—Weak solutions of boric acid, potassium chlorate, or potassium permanganate should be employed. The lesions may be touched with dilute tincture of iodine or the tincture of chloride of iron.

Koplik's spots in measles, the strawberry tongue of scarlet fever, and analogous conditions are described under the respective diseases.

TUBERCULOSIS OF THE MOUTH

This is rarely primary, although clinically, cases occur in which, aside from the oral or salivary tuberculosis, no other tuberculous lesion is demonstrable. In the tonsils an apparent primary localization of tuberculosis has been described.

Tuberculosis in the form of *lupus* may spread from the face to the mouth. The ordinary form of tuberculosis is usually the result of a direct infection of the mouth with bacteria from the sputum. If there is a hematogenic infection, it has not been demonstrated. It is not likely that this occurs in the tongue, as muscle tissue in general is seldom affected by tuberculosis. Tuberculosis of the *lips* is occasionally seen in tuberculous subjects. It assumes the form of an ulcer, which is not easily distinguished from chancre.

Miliary nodules may appear on the flesh of the *gums;* ulceration may occur along the free edge and extend to the hard palate. The condition

has followed tooth extraction in tuberculous subjects. Tuberculosis of the *soft palate* sometimes occurs in persons with pulmonary tuberculosis.

The *tongue* is the commonest seat of oral tuberculosis, the lesion being due to infection from the sputum. Cases are recorded in which the sputum did not seem to be the cause of infection; but in which the latter came from without. The only instance seen by the writer occurred in a street-car conductor, who had the habit of wetting the transfer tickets with his tongue, so as to be better able to separate them with his fingers. Morrow and Miller[1] report 14 (1 per cent.) cases of secondary tuberculosis of the tongue in a series of 1440 tuberculous patients.

The disease appears in one of several forms, as circumscribed submucous nodules (tuberculomas), which in time ulcerate, as a disseminated process, and rarely in the form of tuberculous fissures or rhagades. The nodules are either single or multiple, and may remain stationary for a long time. Eventually, ulcers form which are shallow, irregular in outline, have undermined edges, and are covered with a grayish-white slough; toward the margin miliary nodules may be seen. Ulcers occurring in association with advanced tuberculosis of the lungs have a greater tendency to spread in extent and depth than those that are apparently primary. The lymph glands are rarely affected. There is not much pain in the usual chronic non-spreading or slowly spreading ulcers.

Diagnosis.—A careful history and discovery of tuberculosis elsewhere aid materially. In differentiating tuberculous and carcinomatous ulcers, the following points are important: tuberculous ulcers may be multiple; the edges are softer and less infiltrated; there is less pain, and less frequent involvement of the lymph glands than in carcinoma; the age of the patient is also of importance.

Treatment.—If the pulmonary disease is far advanced, treatment is hardly worth while. In other cases, total excision of the tuberculous area is the best procedure. If not possible, the ulcers may be removed with the thermocautery or sharp spoon. For the dressing of the ulcers, iodoform is best.

SYPHILIS OF THE MOUTH

In the clinical course of syphilis, lesions of the mouth occupy a prominent place. The *primary sore* is found there in the largest number of cases of so-called extragenital syphilis. The lesion may be only a fissure or a superficial flat erosion, with a pseudomembranous covering. It is usually single, and, even if small, leads to marked glandular enlargement. Its commonest sites are the lips, especially the lower, the tongue, the hard and soft palate, and the tonsils. The danger of infection to others renders it important to make a correct diagnosis early. This is well illustrated by the epidemic of chancre of the lip from kissing reported by Schamberg,[2] in which a man gave chancre of the lip to eight persons. If it is a case of syphilis insontium, the patient is generally unaware of the nature of his ailment. In the diagnosis tuberculous and cancer-

[1] *Jour. Am. Med. Assn.*, 1924, **83**, 1484.
[2] Ibid., 1911, **57**, 783.

ous ulcers have to be considered. The demonstration of the *Treponema pallidum* in smears from the ulcer facilitates the diagnosis.

Secondary Lesions.—The secondary lesions in the mouth are an erythema and the so-called mucous patch. The latter, which is among the most infectious of the syphilitic lesions, is a pearly or milk-white area upon a red inflamed surface. The patches are irregular in outline, and variable in size and number. They are found in all parts of the mouth, most frequently upon the lips, the palatal arches, and the tonsils. At the angles of the mouth they lead to rhagades. They appear about the same time as, or before, the roseola on the skin and may be painful or painless. The diagnosis is not always easy; leukoplakia is to be excluded by its chronicity and by its not occurring on the tonsils and soft palate, as well as by the Wassermann and therapeutic tests.

Treatment.—The local treatment consists in the use of antiseptic washes in the mouth and direct application of 1 per cent. mercuric chloride solution, of a solution of nitrate of silver (10 to 20 per cent.), or chromic acid solution (5 to 10 per cent.). It is best to use wooden applicators and tongue depressors, and burn them afterwards.

Tertiary Lesions.—Tertiary lesions in the mouth are of the nature of gummata and require no special description. Their most frequent sites are the hard and soft palates; but they may be found in the tongue, lips, and rarely in the cheek. In the palate they usually lead to perforation. The tertiary lesions of the tongue may, according to Fournier, be divided into two types—sclerosing and gummatous glossitis. In the former the infiltration does not break down, but cicatrizes and gives to the tongue a nodular or puckered appearance (langue lobée, langue rhagadiforme). The gummatous lesions break down and ulcerate. A teritary lesion may be mistaken for a primary sore, but, besides being usually deeper, it is not accompanied by marked adenopathy. The history, moreover, is helpful.

Treatment.—The treatment consists in the vigorous use of arsphenamine and of mercury and potassium iodide.

Hutchinson's Teeth.—A crescentic notching of the upper central incisors with a peg shape was described by Jonathan Hutchinson as a sign of congenital syphilis. It is found in the permanent set, and disappears with advancing years through the wearing down of the edges of the teeth. Seldom is the regular crescent found in conditions other than syphilis, and the presence of such teeth always suggests a careful search for additional evidence of congenital lues.

ACTINOMYCOSIS OF THE MOUTH

Actinomycosis is caused by the *Actinomyces bovis* which is said to gain entrance through decayed teeth or an injury to the mucous membrane of the gum through an abrasion produced by chewing straw carrying the fungus. In some instances one of the salivary glands becomes the seat of primary infection.

The *symptoms* are insidious in onset, a slowly developing swelling making its appearance, usually painless. This tumor is often attended

with considerable induration of the surrounding tissue, out of proportion to the size of the lesion. The patient may think he is suffering from a simple chronic alveolar abscess, although insidious penetration of the jaw has already taken place and small sinuses exist in which the typical ray-fungus granules are found in the exuding pus. Early in the disease there is little fever and constitutional disturbances are often minimal. The tongue and the soft tissues of the mouth may be involved. Multiple sinuses may discharge on the external surfaces of the jaw. The lymphatic glands in the neck become swollen, with a peculiar stony hardness surrounded with considerable amount of œdema. As the disease advances cachexia develops.

The *diagnosis* may be difficult but in any case where sinuses of long duration are found perforating the gums and the buccal mucosa the possibility of actinomyces should be borne in mind and search made for the typical ray-fungus granules which are easily identified. Roentgen-ray photographs of the jaw are most useful. The *treatment* is early and efficient surgery, combined with the internal administration of iodide and the use of a streptothrix antigen. Roentgen-ray therapy has yielded excellent results in some cases.

LEPROSY OF THE MOUTH

This affects the mouth and tongue only secondarily. It appears in the form of nodules, which, in the tongue, may be symmetrically situated on both sides of the raphé; by their coalescence, extensive infiltrating plaques may be formed. Ulceration is rare. The histological lesions are like those of leprosy elsewhere.

SCLEROMA OF THE MOUTH

This reaches the mouth through the posterior nares, and produces infiltrated areas covered with a somewhat bluish-red mucosa. After a time very hard nodules appear that are not usually spontaneously painful, but somewhat tender on pressure. They scarcely ever suppurate, but may become superficially ulcerated. The infiltration consists of two layers—an upper vascular layer and a lower rich, in cells and traversed by fibrous bands, to which the extreme hardness is due. The similarity to a round-celled sarcoma is quite marked.

THE TONGUE

The coating of the tongue hardly has the diagnostic value attached to it by the older clinicians. Nevertheless, it gives much information and a study of it should not be neglected. It may depend upon local conditions in the mouth or nasopharynx; upon causes arising from the gastro-intestinal canal; or upon general conditions. A heavy coating is compatible with good health, and the clean tongue is not always a sign that the alimentary canal is performing its functions properly.

Some persons have a furred tongue on slight provocation, while others, in severe affections, do not. The tongue is usually heavily coated in persons with restricted movements of the jaw.

An exclusive milk diet nearly always produces a coating of the tongue, probably chiefly because of the suspension of the masticatory movements. In some persons even a single glass of milk will give rise to this condition. A coated tongue is found in mouth breathers, in fevers, and in some forms of dyspepsia. In hyperchlorhydria the tongue is usually dark red, moist, and clean; it is also at times remarkably clean and red in diabetes mellitus. It is pale and heavily coated in anacidity and clean in gallstone disease often when gastric symptoms are marked.

Anomalies.—*Aglossia*, a total absence of the tongue, is extremely rare. There is indeed only one indubitable case, that of Jussieu (Rosenthal).[1]

Microglossia, smallness of the tongue, is likewise rare.

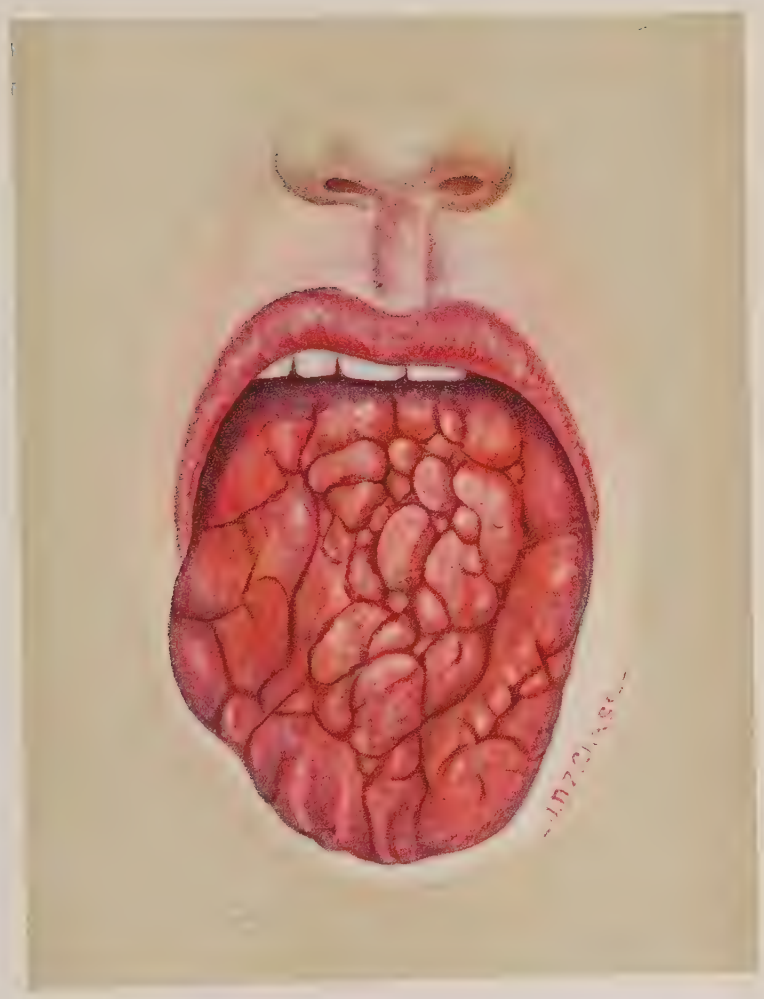
Macroglossia, large tongue, is usually applied to enlargements of the tongue not due to acute inflammation, and is of four varieties: (*a*) Lymphatic (lymphangioma); (*b*) cavernous (hemiangioma); (*c*) muscular or parenchymatous, the rarest, of which Helbing[2] reports a case; (*d*) neuromatous macroglossia, of which cases have been described by Abbott and Shattock[3] and Wagner.[4] A chronic enlargement, due to syphilis, might be added. Funk[5] reported a case of *cavernous angioma* of the tongue and reviewed the literature. He states that the condition is rare. The symptoms are dependent upon the degree of enlargement, pressure, obstruction to breathing and interference with the function of the organ. Hemorrhage may occur from trauma, such as biting the tongue. The treatment is surgical, by roentgen-ray or radium. Macroglossia is generally bilateral, but may be unilateral, as in the case of Little,[6] in which it was probably due to congenital syphilis; and in that of Maas, in which it was associated with congenital hypertrophy of one-half of the body. The chief causes of macroglossia are cretinism and syphilis; the former producing especially the lymphangiomatous form, which may be associated with *macrocheilia*, large lip. In the cases due to cretinism, thyroid extract might be useful. In a case reported by Comroe[7] a cure was brought about the excision of a V-shaped piece.

Doubling of the tongue, excessively long tongue, and *bifid* tongue have been described, but are unimportant.

Congenital deformities of the frenum are supposed to be common, and to the so-called tongue-tie the laity ascribe delayed talking and difficulty in sucking. Cutting of the frenum is, however, very rarely necessary, although Makuen has reported a case of rapid speech development in an adult following the operation for tongue-tie. In a case of the writer's, a trained nurse, the tongue-tie prevented protrusion of the organ but did not materially interfere with speech.

[1] *Die Zunge*, 1903, p. 17.
[2] *Jahrb. f. Kinderh.*, 1895, to 1896 **41**, 442.
[3] *Annals of Surgery*, 1903, **37**, 321.
[4] Cited in *Ztschr. f. d. gesam. Med. u. i. Grenzgeb.*, May 26, 1913.
[5] *Jour. Am. Med. Assn.*, 1922, **79**, 1113.
[6] *British Jour. Dermat.*, 1906, **18**, 181.
[7] *Cleveland Med. Jour.*, 1911, **10**, 743,

PLATE V



Syphilitic Lobulation of the Tongue. "Cobble-stone Tongue."

PLATE VI

Bleeding Tongue in Hysteria.

Tongue swallowing may occur if the frenum is too long. The tongue may roll back and so press against the posterior wall of the pharynx that the entrance to the larynx is occluded and suffocation results.

Tongue sucking is especially common in Mongolian idiots. It leads to marked fissuring of the tongue and to enlargement of the papillæ.

Scrotal tongue (langue scrotale) is a term much used by the French to describe a fissured tongue resembling the scrotum in its roughness. It is difficult to find an explanation for it, although sometimes there is a history of gastro-intestinal disorders. Some of the patients in early life were arthritic subjects. The condition may run in families.

Black Tongue.—*Synonyms:* Lingua nigra; nigrities linguæ; hyperkeratosis of the tongue; melanotrichia of the tongue; melanoglossia; German—Haarzunge. This is a condition in which a brownish or black patch appears on the posterior portion of the tongue, in the neighborhood of the circumvallate papillæ. It is either smooth or covered with densely intertwined hair-like processes varying in length up to 1 cm. The hairs are elongated filiform papillæ that have become pigmented and cornified. Some hold that the black discoloration is due to a mould; but Blau found no mould in four cases. The causes of black tongue seem to be various. Heidingsfeld[1] thinks that the true or permanent cases have a congenital origin and are due to some anomaly of development. The spurious cases of black tongue are caused by local or general irritating or infectious agencies, such as tobacco, syphilis, antiseptics, etc. A parasitic origin has not been established. It has been found in syphilis, diabetes, neuralgia, etc. It may come and go without treatment, and this suggests that it depends upon changes in the salivary secretion. There are usually no subjective symptoms.

Varicose Veins of the Tongue.—Dilatation of the ranine veins on the under surface of the tongue is not uncommon; but the veins on the dorsum may also become varicose, especially those running from the base forward to the circumvallate papillæ. The causes are local.

Hemorrhage from the Tongue.—Bleeding tongue, glossorrhagia. This is most often traumatic, but may occur in purpura and other hemorrhagic conditions, and in hysteria, of which the writer has seen a striking example. (See Plate VI.)

Paralysis of the Tongue.—Glossoplegia. This may be due to central or peripheral lesions of the nervous system, and is either unilateral or bilateral. Unilateral glossoplegia may be caused by disturbance of one of the hypoglossal nerves; it is also present in the majority of cases of cerebral hemiplegia. The tongue is deflected toward the paralyzed side. The chief cause of bilateral glossoplegia is progressive muscular atrophy.

Spasm of the Tongue.—The tongue participates in the general muscular commotion in epilepsy, chorea, etc. Spasm limited to the tongue, a sort of tic, has been described; spasm of the facial and masticatory muscles may be associated with it. Some cases of spasm are hysterical; in some no definite cause is discoverable.

[1] *Jour. Amer. Med. Assoc.*, 1910, **55**, 2117.

Paralysis of the Soft Palate.—This, like glossoplegia, may be unilateral or bilateral. In the unilateral form the palate on the affected side hangs lower than on the normal side. In bilateral palsy the entire palate droops and is motionless during speaking and breathing; speech and swallowing are disturbed, and food regurgitates through the nose. The most important causes are neuritis following infectious diseases, especially diphtheria; bulbar palsy, tumors at the base of the brain in the posterior fossa; aneurism of the vertebral artery; and tabes dorsalis.

Glossitis.—Acute inflammation may be due to biting of the organ during an epileptic convulsion, biting by insects, burns, or to the irritation of a rough, carious tooth. An acute glossitis occurs in smallpox, erysipelas, scarlet fever, and typhoid fever, and usually accompanies severe forms. Tobacco may also cause glossitis and is responsible for the so-called smoker's patch.

Symptoms.—The affected side of the tongue swells and at the point of injury becomes covered with a grayish-white membranous deposit. The swelling may be so great that the tongue hangs out of the mouth. Pain and discomfort are severe and mastication may be impossible. The saliva is increased in amount and is sticky. The condition usually terminates in resolution but in some cases suppuration ensues. When unilateral in the beginning (hemiglossitis), it rarely spreads to the other side.

Treatment.—Antiseptic mouth washes are indicated. In severe cases, and when abscesses form, a long, deep incision must be made into the substance of the organ.

Chronic Streptococcal Glossitis.—A persistently painful tongue, not due to abrasions, injury, trauma or irritation from jagged teeth, or ill fitting dentures or syphilis, malignant conditions or tuberculosis, is caused by streptococci. This condition is important as it is not usually recognized and frequently diagnosed as neuralgia of the tongue or part of a neurosis. The error occurs because there is usually no physical sign present. In the beginning the patient complains of a more or less small area of discomfort at the tip or along the sides of the tongue which frequently spreads to the entire tongue. The patient experiences pain on chewing and speaking. Spicy, acid, hot foods and liquids greatly add to the pain and the patient avoids them. The sense of taste becomes abnormal. The patient complains bitterly, and may wander from physician to physician in search of relief. Ulceration and exudate are not present. Fissures, if present, are slight and occur late in the condition. Physical examination discloses no evidence of disease. The pain is believed to be due to a streptococcal infection of the nerve endings beneath the epithelium of the tongue.

Treatment.—Because of difficulty in relieving the symptoms except in the early stages of the disease, its early recognition is important. The usual mouth washes have not afforded relief. The occurrences of streptococci in the subepithelial layer explains the failure of the local application of silver preparations, arsphenamine locally, and like remedies. Goss recommends the use of a mouth wash of chlorine water diluted with sufficient water to be bearable, bathing the tongue well before the antiseptic

is expelled. The tongue is prepared by thoroughly drying it when protruded with antiseptic gauze, before the chlorine water is used. Streptococcal serum locally and a long course of autogenous vaccine therapy have been used with success. Roentgen-ray and radium applications may prove beneficial.

Moeller's Glossitis; Glossodynia Exfoliativa; Chronic Superficial Glossitis.—This is a very painful affection of the tongue, characterized by bright-red lines or patches at the margin and tip. The pain, which is the principal symptom, is out of proportion to the local lesion, and is much increased by chewing and speaking. The disease chiefly affects women, especially those who are weak and decrepit. The cause is unknown. The only instance seen by the writer was in a woman with pernicious anemia. Local treatment was of no avail; the roentgen-ray and applications of nitrate of silver were tried without effect. With an improvement in the blood the condition subsided, but recurred; the patient eventually died of anemia.

Papillitis Lingualis; Linguopapillitis.—This is a painful condition of the tongue, which reveals nothing to the naked eye, but the magnifying lens shows small, ulcerating points hidden in the folds of the mucosa about the fungiform papillæ of the tip and margin of the tongue.

Treatment.—The painful points should be touched with the galvanocautery, aided by a lens.

Ulcer of the Frenum.—Ulcer is most common in children suffering from whooping-cough, and is due to the forcible protrusion of the tongue and impact of the frenum against the teeth during the paroxysms.

Glossitis Papillosa Acuta; Glossitis Papillaris.—This is an inflammation limited to the circumvallate papillæ, and is characterized by slight difficulty in swallowing, burning, and sticking sensations in the throat, and an irritative cough. An acute form has been described by Michelson.[1] Stetter,[2] under the name of glossitis papillaris, reports four cases with histological studies. Tuberculosis may produce conditions very similar to the ones described.

Wandering Rash of the Tongue.—*Synonyms:* Geographical tongue; exfoliatio areata linguæ; état lichenoide; annulus migrans; Zungenfratt; état tigré; glossitis exfoliatricans marginata; desquamation en aires. This interesting condition of the tongue is characterized by circinate, crescentic, or circular patches in which the epithelium is desquamated. The patches may be multiple or single, they may affect the dorsum or the margin of the tongue and are bordered by a slightly elevated, whitish ring which is sometimes double-contoured. When the patches are multiple and affect a large part of the tongue the fantastic shapes give a remarkable appearance well described in the name *geographical tongue.* The patches may come and go suddenly; their shape and size may alter rapidly. Contiguous patches may fuse. In some cases a single patch may remain for a long time unchanged.

Etiology.—The cause is not definitely known. Gastro-intestinal disorders and heredity are possible factors. A single patch may be due to a sharp tooth. Syphilis is not responsible for the condition.

[1] *Berl. klin. Wochnschr.*, 1890, **27**, 1094. [2] *Arch. f. klin. Chir.*, 1898, **56**, 324.

Histological examination shows a superficial desquamation of the epithelium, the latter being replaced by a coagulated exudate containing leukocytes and degenerated epithelial cells. The cells of the deeper layers of the mucosa are in a state of cloudy swelling. Some authors have found the changes most marked in the lower strata of the mucosa.

Symptoms.—There are usually no subjective symptoms except a little burning or sensitiveness. The affected area looks paler and smoother than the surrounding parts. The lymphatic glands may be enlarged; in women the condition is apt to be worse at the menstrual periods. Some patients, fearing cancer, become hypochondriacal.

Treatment.—It usually subsides without treatment. Attention should be given to the gastro-intestinal canal. The patient's mind should be put at rest as regards cancer. A mouth-wash of sodium hyposulphite and glycerin, of each 10 parts, and water 180 parts, may be used.

Glossodynia.—Pain of the tongue, without gross lesion to account for it, is not uncommon; usually the pain is referred to the anterior third of the organ or along the margin of the tip. It is often difficult to ascertain the cause; but in a search for it the classification of Chaveau[1] may prove helpful. He names the following varieties:

1. Glossodynia secondary to trigeminal neuralgia, especially of the inferior dental branch of the trigeminal.
2. Glossodynia of the insane, usually starting as a local paresthesia.
3. Glossodynia of tabes, corresponding to the crises in other organs.
4. Glossodynia of hysteria.
5. "Rheumatism" of the lingual muscle or rheumatic glossodynia.
6. Glossodynia attributable to local causes. These may be extrinsic or intrinsic. Among the extrinsic causes are (*a*) dental affections and artificial teeth (causing papillary hypertrophies and other lesser lesions); (*b*) granular pharyngitis and hypertrophy of the posterior pillars, and of the lingual tonsil, etc. Among intrinsic causes are mentioned (*a*) lingual varices; (*b*) chronic glossitis from tobacco, alcohol, spices, iodine, lead, gout, etc., and (*c*) papillary hypertrophy.

Leukoplakia.—*Synonyms:* Leukoplasia; psoriasis linguæ; tylosis linguæ; ichthyosis buccalis; keratosis buccalis; smoker's patch. This is a chronic disease of the mucous membrane of the tongue, rarely of the lips, cheek, palate, and gums, characterized by thick, elevated, indurated, whitish patches having either a fissured or more rarely a smooth appearance.

Etiology.—There is a connection between syphilis and leukoplakia, but that the former is the cause cannot be maintained, in view of the investigations of Erb[2] and Neisser.[3] Nevertheless, the frequency of a history of syphilis, in 65 per cent. of the cases of leukoplakia, according to some authorities seems to justify the contention that leukoplakia is a parasyphilitic lesion. Smoking is an important factor, and explains in a measure the predominance of the disease in the male sex. Of Pulvermacher's 54 patients, only 1 was a woman. The use of spices, condiments,

[1] *Arch. gen. de Med.*, 1900, ann. 77, n.s., **3**, 66.
[2] *Münch. med. Wchnschr.*, 1892, Nr. 42.
[3] Quoted by Mikulicz and Kümmel, *Die Krankheiten des Mundes.*

and alcoholic beverages must be mentioned among the possible causes, likewise irritation by carious teeth and badly fitting dental devices. As leukoplakia has been found associated with diseases of the skin characterized by scaling and keratosis, it may be looked upon as an expression of a general tendency to hyperkeratosis, which in the mouth is excited by frequently repeated or long-continued irritation of various kinds. The most common dermal association is psoriasis.

The disease is most common in the male sex and in adult life, although Hartzell reports a case of extensive leukoplakia associated with keratosis of the skin in a young girl aged eleven years. The disease progressed steadily until at the age of twenty-six there was carcinoma of the tongue.

Pathology.—The principal feature is a hyperkeratosis of the mucous membrane. The epithelium, especially the corneous layer, is greatly thickened. The subcorneous stratum contains many cells filled with eleidin droplets and granules. Mitotic figures are abundant in the deeper layers of the rete mucosum; while the elongated papillary processes are extensively infiltrated with leukocytes.

Relation to Epithelioma.—The transformation of leukoplakia into cancer is indubitable. This is not a complication or an accident, but a distinct evolutionary development, the causes of which reside in the histogenesis of leukoplakia. It occurs in about 20 per cent. of the cases.

Symptoms.—In the early stages leukoplakia appears in the form of deep-red erythematous patches, which after a short time assume a bluish-white color, looking as if the mucous membrane had been painted over with a strong solution of silver nitrate. Gradually the patches become thicker and larger, and, in the case of the tongue, may cover the mucosa so completely that the papillæ are no longer visible. The parts affected are in the order of frequency: tongue, lips, cheek, gums, and palate. The pharynx and the base of the tongue posterior to the circumvallate papillæ are rarely involved. The patches may be smooth, more often they are fissured. To the touch they have a tough, leathery feel. The superficial layer can at times be picked off easily without much bleeding being produced; regeneration quickly takes place.

The subjective symptoms are slight, unless the fissures are deep and raw, in which case there may be pain on chewing. The patient who is aware of his leukoplakia is apt to become hypochondriacal, fearing either cancer or that syphilis is returning under a new form.

Treatment.—This avails but little, and it is doubtful whether it is possible to prevent by any form of application the development of carcinoma. Cleanliness of the mouth, cessation of smoking, abstention from irritant spices, and the removal of sharp-edged teeth are important. Antiseptic treatment and strong caustics more often do harm than good. A 10 per cent. solution of tincture of iodine has been recommended, and Hartzell advises applications of salicylic acid (1 to 100 or 150). The roentgen-ray cautiously employed has been of some value in the hands of Hartzell and Schamberg. Bockhart had success with the following local treatment: the diseased areas were rubbed once a day or once in two days with balsam of Peru; in addition the mouth was rinsed from six to twelve times a day with from ½ to 3 per cent. salt solution. He considers the saline washing more important than the application of the balsam.

Smooth Atrophy of the Tongue.—This is an atrophy of the epithelial covering and of the large sebaceous glands at the base of the tongue, which is found more often in acquired *syphilis* than in any other condition, and has been considered a pathognomonic sign of this disease. Goldschmidt[1] found it in 17 per cent. of 140 cases of secondary, and in 47 among 60 cases of tertiary syphilis. But as it is also found in non-syphilitic subjects, it cannot have the diagnostic value ascribed to it. L. S. Milne[2] found it 39 times in 505 autopsies (25 male, 14 female). Among 36 syphilitic cases, it occurred 14 times, a sufficiently large proportion to make the relation significant. It was also found a few times in tuberculosis. In examining for it, the finger or the mirror may be used. With the former, the unnatural smoothness of the base of the tongue is perhaps more readily detected.

Riga's Disease.—*Synonym:* Produzione sottolinguale. This is a benign tumor-like excrescence on the lingual frenum of infants. It is most common in Italy, whence nearly all the observations and studies have come. Good accounts, with bibliographies, are found in the articles of Ernst Deutsch[3] and E. Audard.[4] The cause is in dispute, but in some cases it is of mechanical origin (decubital), due to irritation by the lower incisor teeth. Histologically, it is a papillomatous growth.

Symptoms.—The disease appears between the ages of three and eighteen months and is equally common in both sexes. It is probably not contagious; some Italian writers, however, consider it so. It lasts from two weeks to two months; although some cases are on record that persisted for from eighteen to twenty months. It must be distinguished from the ulcer of whooping-cough, chicken-pox, syphilitic ulceration, herpes, and impetigo.

Treatment.—If a cause is discoverable, it should be removed. If there is irritation by teeth, they should be extracted. In persistent cases, caustics, silver nitrate or tincture of iodine, may be applied, or the growth may be excised.

Tumors.—*Fibroma*, usually of the hard variety, is found on the surface or in the substance of the organ. *Sarcoma* is a comparatively rare tumor, generally spindle-celled, and occurs in the substance of the tongue.

Thyroid Tumors.—A small tumor is sometimes found at the base of the tongue in the region of the foramen cæcum, which histologically is made up of tissue closely resembling that of the thyroid gland and the origin of which is to be traced to the remains of the thyroglossal duct. Glas[5] reported a case of adenomyoma occurring in the same region as the thyroid tumor, traced to the remains of the ductus lingualis.

Carcinoma is the most frequent tumor found in the tongue. It is commoner in the male sex (66 to 3 in the statistics of Meller), and extremely malignant. Patients not operated on usually die in less than a year after the appearance of the first symptoms.

Amyloid tumor is rare; an example is recorded by Gross.[6]

[1] *Berl. klin. Wchnschr.*, 1899, Nr. 43. [2] *Jour. Am. Med. Assn.*, 1911, **57**, 1040.
[3] *Arch. f. Kinderh.*, 1905, **40**, 168.
[4] *Rev. mensuelle des mal. de l'enfance*, 1902, **20**, 49.
[5] *Berl. klin. Wchnschr.*, 1905, **18**, 746. [6] *Deut. Zeit. f. Chir.*, 1906, **84**, 462.

THE SALIVARY GLANDS

The normal saliva is composed of the secretions of the salivary glands—the parotid, submaxillary, and sublingual—and of the mucous glands of the mouth. It is a watery, opalescent, slightly stringy fluid, of a feebly alkaline reaction, and has a specific gravity of from 1002 to 1008. Its principal organic constituents are mucin—a diastatic ferment—ptyalin, oxydases, and slight traces of protein. Urea, according to some authorities, is also present. Among the inorganic constituents are potassium and sodium chloride, potassium sulphate, sodium carbonate, calcium carbonate and phosphate, potassium sulphocyanide, and carbon dioxide. The total solids amount to from 5 to 10 parts per 1000. The freezing point is 0.20° C. Apart from the fact that the protein is a glycoprotein, nothing definite is known of its nature. The potassium sulphocyanide content varies considerably. In smokers it is said to be greater (0.2 per 1000) than in non-smokers (0.03 or 0.04 per 1000).

The *secretion* of the saliva is under the control of two sets of nerves: one from the brain, the other from the sympathetic system. In the case of the submaxillary gland, the cerebral impulses are conveyed by fibres of the facial nerve running in the chorda tympani. Studies on animals have shown decided differences in the saliva following separate stimulation of these two types of nerve fibres. The *sympathetic saliva* is scantier, thicker, and richer in solids, particularly in mucin, than the *chorda saliva*. A third variety of saliva is the so-called *paralytic saliva*, which follows poisoning with curare or section of the gland nerves. The normal daily quantity of saliva varies from 1400 to 1500 cc.

The reaction, usually alkaline, is subject to variations. It may be acid or neutral even in health; in diabetes, fevers, and dyspepsia it is often acid. In making tests, the possibility of acid mouth washes being used should not be overlooked. The relative proportion of organic as well as inorganic constituent changes in response to variations in the stimulus. Von Zebrowski has shown that the quality of the excitant and intensity of its action, as well as the locality and manner of its application, are of importance. The secretion of saliva is stimulated more by those substances that require longer chewing. In unilateral mastication, the gland on the active side is especially stimulated; the opposite gland also secretes, but more slowly, and the saliva contains a somewhat larger amount of organic substances.

Stern and Lederer,[1] in a study of the saliva in 158 cases of diabetes mellitus, found the quantity increased in 8, diminished in 89, normal in 63. The reaction was acid in 47, alkaline in 92, neutral in 8. Glucose was found in 85. The diastasic quality was unchanged in 90 per cent. When the sugar disappeared from the urine it also disappeared from the saliva. In acute gastritis an acid secretion was found in 8 out of 20 cases, being caused in 2 by lactic acid and in 2 by acetic acid. In hyperchlorhydria an increase of secretion was found in 27 out of 182 cases; the

[1] *Jour. Am. Med. Assn.*, 1904, **43**, 1765.

reaction was acid in 71, alkaline in 41, neutral in 5, amphoteric in 65. The acid reaction was due to lactic acid in 12, to acetic acid in 12, to lactic and acetic acids in 9, to hydrochloric acid in 6. In pyloric stenosis the reaction was acid in 5, alkaline in 8; in hypochlorhydria the reaction was acid in 2, alkaline in 15, and amphoteric in 6. Urea is increased in severe nephritis and in uremia.

1. **Increase of salivary secretion** (hyperptyalism, ptyalism, salivation, sialorrhœa, sialosis) is often apparent rather than real, the saliva, normal in amount, not being swallowed. This is the case in paralysis of the muscles of deglutition, or of those of the lips and tongue; in quinsy and other forms of tonsillitis, and in severe types of pharyngitis, when swallowing is painful. True hyperptyalism is a condition in which more than the normal amount of saliva is secreted. Its causes are various:

(*a*) *Local.*—The different forms of stomatitis; dentition; and chorea, by reason of the active masticatory movements.

(*b*) *Reflex.*—Hyperchlorhydria; gastric ulcer; nausea; pregnancy; trigeminal neuralgia; helminthiasis; pancreatic calculus; pain from various sources. The most profuse salivation ever seen by the writer occurred in a man who had been operated upon for hernia. No tangible cause aside from the operation could be found. In a woman, suspected of being a morphine habitué, there was a constant flow of a sticky saliva while she was under surveillance and could not obtain the drug. The salivation subsided immediately after a small morphine injection.

(*c*) *Direct nerve stimulation,* either central or peripheral; migraine; bulbar palsy; uremia; certain poisons, as, for example, mercury. The salivation in the last-named is only in part due to stomatitis, for it often precedes inflammatory changes in the mouth. Certain drugs, such as pilocarpine, act through direct stimulation of the nervous system. Hysterical and neurotic salivation, which in some cases depend on direct nervous influences may also be reflex.

Salivation in Children.—Salivation is normal in infants; it is increased by dentition, but is not dependent upon it. Salivation is present in all forms of stomatitis, and, without any local changes in the mouth, in cretinism and idiocy. Jordan reported two cases of "idiopathic salivation" in children. The dribbling began during dentition and continued, without any apparent cause, after the process had stopped.

2. **Diminution of secretion** (hypoptyalism, aptyalism, absence of secretion) occurs in fevers, especially in pneumonia, typhoid fever, and septic fevers; after the use of atropine; in fright and excitement (the rice ordeal); in loss of fluid through diarrhœa or the elimination of dropsical effusion; in cirrhosis of the liver when ascites is forming, and in atrophy of the salivary glands. The writer has also noticed an annoying dryness in arteriosclerosis with great hypertension and polyuria, with and without thirst.

Xerostomia.—Under the name of xerostomia, or dry mouth, Jonathan Hutchinson[1] described a condition of distressing dryness due to suppression of the salivary secretion. It is most common in women (32

[1] *Clin. Soc. Trans.*, 1888, **21**, 180.

women to 4 men, in Hall's table),[1] and usually resists treatment. In a case of the writer's, a woman aged thirty-eight years, the dryness had lasted two years, and was so great that the patient had to rise two or three times a night to wet her mouth. The urine amounted to two liters a day, had a low specific gravity, 1008, and was free from albumin and sugar. There were also darting pains in the tongue (glossodynia), and her speech was somewhat disturbed. In other cases reported, mastication and swallowing were affected.

The tongue and mouth are dry, red, and glazed, and there seems to be suppression not only of the salivary secretion, but also of that of the buccal glands. In 8 cases of 39 (Hall) the parotids were enlarged. The disease began suddenly in 6; in 6 it followed mental shock, and in 4 influenza or other slight febrile affections.

Etiology.—The condition is in the majority of cases best explained on the basis of a disturbance of the nerve centres controlling the secretion of the salivary and buccal glands. In some instances it may be due to a primary affection of the salivary glands, since it is present in the so-called Mikulicz's disease. Zagari[2] found atrophy of the parotid and submaxillary glands (histologically determined) in a case of xerostomia in a woman aged fifty years, who had died of a gradually increasing emaciation and marasmus.

Treatment.—The condition has generally proved rebellious to treatment. The mouth should be kept clean. The free use of liquid petrolatum or glycerin is beneficial in keeping the mouth moist. The galvanic current is worth a trial, and pilocarpine in small doses may also be employed.

Acute Inflammation.—Acute inflammation of the parotid gland—parotitis—appears in two forms: the epidemic parotitis or mumps, and the so-called secondary parotitis, which is found associated with typhoid and septic fevers, pneumonia, dysentery, pyelitis, smallpox, measles, scarlet fever, and is also seen at times after abdominal operations, especially oöphorectomy. As far as the writer's observation goes, it is most common with diseases situated below the diaphragm. In obscure febrile cases the appearance of a parotitis should lead the physician to consider carefully the possibility of typhoid fever, abscess in the pelvis of the kidney, or a perinephritic abscess. The condition has also been called splanchnic parotitis. A parotitis occurring in the course of hemiplegia was described by Gilbert and Villaret.[3] In both cases observed by them the parotid on the paralyzed side was affected.

Parotitis Due to Drugs.—The writer has seen an acute enlargement of the parotid gland following the administration of potassium iodide; it may also occur as a complication of lead poisoning.

Chronic Inflammation.—Chronic inflammation usually depends on retention of salivary secretion, and is most common in the parotid. The gland is enlarged and hard, and may resemble a malignant tumor. The disease is attributable to an infection propagated from the buccal cavity, and is often associated with the presence of stones in the ducts or the

[1] *Quart. Med. Jour.*, 1898–99, **7**, 26.
[2] *Il Policlinico*, 1907, **14**, Medical Section.
[3] *Sem. méd.*, 1906, p. 104.

glands themselves. The size of the gland varies according to the degree of obstruction and retention.

Sialodochitis Fibrinosa.—Under this name Emden[1] reports the following case: A woman, aged fifty-four years, suffered at first in long intervals, later, regularly every eight days, from bilateral swelling of the submaxillary and sublingual glands. The attack began with burning pain in the tip of the tongue, was unaccompanied by fever, and produced a firm, dense infiltration of the glands. The whole process subsided after three days, with expulsion from the salivary caruncles of fibrinous plugs, and with profuse salivation. The plugs measured several centimeters in length and branched dichotomously. Emden compares the condition to fibrinous bronchitis, and, while not denying the possibility of a secretory neurosis, attributes it to inflammatory changes in the salivary ducts. Analogous cases have been reported by Naegeli-Akerblom,[2] and by Viaud,[3] who coined the term "whartonitis."

Periodic Swelling of the Salivary Glands.—Certain persons are subject to recurrent attacks of swelling of one or both parotid glands which subsides quickly in a day or two. It is probably due to temporary obstruction of Steno's duct and seems to follow exposure to cold, but may have other causes.

Tuberculosis.—The salivary glands are not often attacked by tuberculosis, a comparative immunity they share with the pancreas. Even experimentally, infection of the glands is not easily accomplished unless their nutrition is first disturbed by trauma. In man tubercle bacilli may reach the glands through the blood, the lymphatics, the excretory duct, or by direct extension from neighboring parts. It is still a question, however, whether in the so-called primary form of tuberculosis the disease is not located in a lymph gland occasionally found embedded in the parotid, from which the disease extends to the parenchyma proper. Mintz[4] collected 8 cases of so-called primary tuberculosis affecting the parotid; and O'Zoux[5] found 4 of the submaxillary. Legueu and Marien, finding in their cases chiefly parenchymatous lesions, concluded that the infection had been propagated along the duct. Bockhorn,[6] Mintz,[7] and Lecéne[8] believe in lymphatic transmission, the principal lesions in their cases having been found in the intra-acinous connective tissue. The infection, whether it travels by the one route or by the other, usually occurs through carious teeth or ulcerated gums about such teeth. Tuberculosis of the salivary glands is of slow development, and is generally mistaken for the so-called mixed tumor.

Syphilis.—This is rare, and has hitherto been found principally in the sublingual gland, occasionally in the parotid gland (Crile). It is usually of the tertiary form, and in the differential diagnosis, which may be

[1] *Sitzungsbericht des aerztl. Vereins in Hamburg*, 1897.
[2] *Monatschr. f. Ohrenheilk.*, 1895, **29**, 80.
[3] *Thèse de Paris*, 1894.
[4] *Deutsch. Ztschr. f. Chir.*, 1901, **61**, 290.
[5] *Arch. clin. de Bordeaux*, 1897, **6**, 28.
[6] *Arch. f. klin. Chir.*, 1898, **56**, 189.
[7] *Deutsch. Ztschr. f. Chir.*, 1901, **61**, 290.
[8] *Rev. de chir.*, 1901, **23**, 524.

difficult, the history, the Wassermann test, and the therapeutic test give the most assistance.

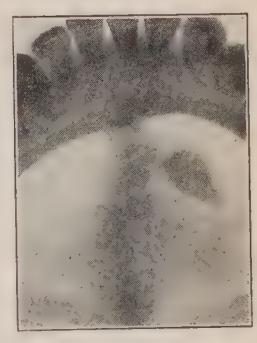
Salivary Calculi.—Stones may form in the ducts, rarely in the glands themselves, the most frequent site being Wharton's duct, at a point from 10 to 20 mm. from the salivary caruncle. They seldom exceed the size of a pea, and are composed chiefly of calcium phosphate or calcium carbonate, which constitutes from 62 to 95 per cent. of the stone. They are usually single, but in the case of Brin there were four in one duct. Duct stones are cylindrical and smooth; gland stones usually round or irregular. The writer has seen 3 cases of salivary calculus, all in women.

Etiology.—Stones formed in the ducts may have a foreign body, such as grains, seeds, bits of food or tartar as a nucleus, but it is probable that the impetus to stone formation is given by bacterial infection. Inflammatory changes in the glands, by bringing about a change in the consistency of the saliva, may lead to stone formation. In several cases there was long-continued irritation of the mouth by a pipe.

Symptoms.—Stones located in the glands do not, as a rule, give rise to marked symptoms, although the gland may be enlarged, firm, and tender. The characteristic feature is an intermittent pain along the floor of the mouth, the so-called salivary colic, which usually comes on during eating and persists for from one to several hours. It is associated with a similarly intermittent tumefaction of the gland and a distention of the proximal part of the obstructed duct. At times there is a purulent discharge (pyorrhœa salivaris) which may be exceedingly offensive. The stone can generally be detected by sounding, by digital palpation, or by means of the roentgen-ray.

Salivary calculi situated on the floor of the mouth may simulate ranula, from which they may be distinguished by noting that in calculus the flow of the saliva is stopped and that a probe cannot be passed along the duct, while careful digital exploration or the roentgen-ray may reveal the concretion. Malignant disease, actinomycosis, and tuberculosis must also be borne in mind.

Fig. 26



Roentgen-ray picture of a salivary calculus.

Treatment. — The treatment consists in the removal of the stone. Sometimes this can be accomplished by pressure and a probe. The writer succeeded by these means in a case in which the concrement was located near the outlet of Steno's duct. When the stone is deep-seated, operation is necessary. In rare instances the stone becomes quiescent and demands no special treatment.

Tumors. — The most interesting as well as the most important new-growth is the so-called *mixed tumor,* which has puzzled pathologists for many years. Clinically, it is a slowly growing, movable, smooth or nodular tumor, usually painless, disfiguring, and often reaching an enormous size. It is more common in the parotid than in any other of the salivary glands, the distribution, according to Boehme, being as

follows: 74.1 per cent. of all cases affect the parotid, 7.7 per cent. the submaxillary, and 1.1 per cent. the sublingual. The skin is rarely adherent. The tumors have a capsule composed of fibrous connective tissue; sometimes nodules of unchanged or inflamed salivary gland tissue are included within the capsule. From the capsule septa extend inward and subdivide the tumor into lobules. The color varies from reddish to yellowish gray. According to the amount of mucoid or hyaline degeneration, the surface is opaque, glistening, or gelatinous; at times cystic spaces are present. If the tumor is malignant, it bursts through its capsule and infiltrates the neighboring tissues; it may cause metastasis in the regional lymph glands, but transference to distant organs is rare. The soft tumors are more malignant than the hard ones, though local recurrence is more common in the cartilaginous forms.

Microscopic studies reveal a very complicated structure, suggesting in some cases carcinoma, and in others sarcoma. Mucoid and fatty tissue and cartilage may still further obscure the picture. In a goodly proportion of cases, in 14 of 26 studied by Ehrich, squamous epithelium is present and may show characteristic horny changes. The cells which constitute the tumor parenchyma proper are arranged in larger or smaller masses resembling gland acini, or in tubules, the lumen of which is lined with cubical or cylindrical cells. It is the origin of these cells that has given rise to most dispute. Some authorities hold that the cells spring from the endothelium of the lymph spaces or perivascular lymph sheaths, and that the tumors must be classed with the endotheliomas and peritheliomas. Küttner,[1] in a study of 97 tumors of the submaxillary gland collected from the literature, found 64 to be endotheliomas, 6 sarcomas, 3 adenomas (?), 5 carcinomas, and 19 of doubtful nature. The endotheliomas may be benign or may resemble sarcoma and carcinoma in the malignancy of their course. Those not having cartilage show a greater tendency to malignancy than the enchondromas.

There are many writers, however, who contend that not only morphologically, but also histogenetically, the tumor cells are epithelial. Given certain conditions of growth, endothelium can easily assume the shapes of epithelial cells. Those tumors in which masses of squamous epithelial tissue are found may, as many have shown, take their origin from remains of the branchial arches. Guleke[2] believes that some of the parotid tumors are teratomas and arise from germinal displacements of the original salivary gland "Anlage;" this latter contributing the cellular elements of the tumor, while the myxomatous, cartilaginous, and osteoid tissue is derived from the remains of the first branchial arch. Wood[3] is also inclined to the view that they arise from embryonic displacements of epiblastic tissue during the process of formation of the parotid and submaxillary glands and the branchial arches. So far as it is possible to decide, those who contend for the epithelial origin have the best of the argument.

Treatment.—This is surgical.

Other tumors of the salivary glands are sarcoma, cases of which are

[1] *Beitr. z. klin. Chir.*, 1896, **16**, 181.
[2] *Arch. f. klin. Chir.*, 1906, **81**, 275.
[3] *Ann. Surg.*, 1904, **39**, 57, 207.

described by Kelly, Lotheissen, and Schridde,[1] lipoma and chondroma. Von Mangoldt describes a cavernoma—a congenital telangiectatic growth, which was found associated with angioma of the overlying skin. An echinococcus cyst has been described.

SYMMETRICAL ENLARGEMENT OF THE LACRIMAL AND SALIVARY GLANDS—ACHROOCYTOSIS, MIKULICZ'S DISEASE

The first complete description of this was given by von Mikulicz.[2] It is a chronic inflammation affecting the salivary and lacrimal glands; but there are cases, evidently of the same nature, in which the salivary glands alone are affected. Blood changes are rare; in some cases, however, the blood presents the picture of leukemia. The lymphatic glands may be enlarged and at times there are analogous infiltrations of the skin. The enlargement of the salivary glands is due chiefly to a diffuse lymphoid hyperplasia, and not to hypertrophy of the parenchyma proper. Von Brunn[3] is of the opinion that the disease is due to an infection carried to the glands in the blood stream and classifies the forms as follows:

I. Cases without blood changes. *A*. Without involvement of lymph glands or spleen. (*a*) Symmetrical enlargement of the lacrimal and salivary glands. (*b*) Symmetrical enlargement of the lacrimal glands alone. (*c*) Symmetrical enlargement of the salivary glands alone. *B*. With enlargement of lymphatic glands and spleen. (*a*) Symmetrical enlargement of the lacrimal and salivary glands. (*b*) Symmetrical enlargement of the lacrimal and salivary glands with infiltration of the skin.

II. Cases with blood changes. *A*. Grave anemia with lymphatic pseudoleukemia and aplasia of the bone marrow. *B*. Leukemia.

Histologically the cases are classified by Hase[4] into three groups:

1. Cases with hyperplasia of the normally present lymphatic tissue.

2. Cases of a chronic inflammatory character presenting tuberculous granulation tissue without caseation.

3. Cases of tuberculous granulation tissue with the presence of tubercle bacilli or positive tuberculin reaction.

A case in a negro has been reported by Ziegler.[5] In children the Mikulicz syndrome is not rare but is usually associated with pseudoleukemia or leukemia. According to Tileston[6] the term Mikulicz disease should be reserved for those cases of chronic painless bilateral enlargement of the salivary and lacrimal glands in which pseudoleukemia and leukemia can be excluded. The cases in the last named disease should be classified as leukemia with the Mikulicz syndrome. Howard's[7] article also contains a good bibliography.

Napp[8] describes a case in a woman aged twenty-seven years, in whom in addition to the enlargement of the lacrimal, submaxillary, and parotid

[1] *Beitr. z. path. Anat. u. z. Allge. Path.*, 1903, **34**, 136.
[2] *Müenchen. med. Wchnschr.*, 1888, p. 759; *Beitr. z. Festschrift f. Billroth*, Stuttgart, 1892, p. 610.
[3] *Beitr. z. klin. Chir.*, 1905, **45**, 225.
[4] *Inaug. Diss.*, Leipzig, 1912.
[5] *New York Med. Jour.*, December 11, 1909; bibliography.
[6] *Am. Jour. Dis. Child.*, 1911, **2**, 293.
[7] *Internat. Clin.*, 1909, **1**, 30.
[8] *Ztschr. f. Augenheilk.*, 1907, **17**, 513.

glands there were submucous nodules on the lips and cheeks and in the conjunctiva. In the conjunctival nodules, which were the only ones examined, tubercle bacilli were found. On the strength of this case, Napp accepts the view that Mikulicz's disease is not a disease but a symptom complex produced by a variety of causes, such as leukemia, a typical lymphomatosis (sarcoma), and tuberculosis. For the treatment of the condition, Pfeiffer recommends the roentgen-ray.

Atrophy.—In addition to the shrinkage of the glands accompanying advancing age (senile atrophy), there is an atrophy of obscure nature that may or may not affect all of the glands simultaneously. In a case of such atrophy reported by Dubreuil-Chambardel,[1] the condition revealed itself by an almost absolute smoothness of the floor of the mouth, and by hollows in the region of the parotid glands. The patient, an otherwise healthy man, aged sixty-one years, complained of dryness of the mouth. The urine was increased in amount to 2000 cc. in a day, but was free from albumin and sugar. Such an atrophy may be the underlying cause in some cases of xerostomia.

LUDWIG'S ANGINA

This is an inflammation—a cellulitis—of the tissues of the floor of the mouth in the submaxillary region. The primary focus is usually some insignificant lesion in the mouth, as a carious tooth, tonsillitis, an ulcer, etc., the infection travelling by way of the lymphatic vessels to the submaxillary lymph glands. In 18 cases studied bacteriologically the streptococcus was found alone in 6 cases, the streptococcus associated with other organisms in 8, the staphylococcus alone in 2, the pneumococcus alone in 1, and an undetermined bacillus in 1. Males are far more often affected than females.

Symptoms.—The disease usually begins acutely, with slight fever, and at times difficulty in swallowing. Coincidentally an indurated swelling appears in the region of the submaxillary gland, on one or both sides which soon extends along the cellular tissue toward the chin, toward the parotid, and down toward the larynx or the sternum. The sublingual tissues form a hard congested swelling arranged like a cushion just inside the inferior maxillary bone, and force the tongue upward and toward the opposite side. The skin over the swelling, during the first four or six days, is movable, then it becomes reddened, œdematous, and adherent; at times there is crepitation. Soon an opening forms in the floor of the mouth through which a thin grayish or reddish-brown fluid is discharged; at the same time the constitutional symptoms become more severe, the fever higher, sleep is disturbed, profuse sweats, delirium, and dyspnœa appear, and the characteristic typhoidal state, due to septic infection, is developed.

Death, in the majority of cases, occurs from invasion of the larynx, the lower respiratory tract, and in some cases of the lungs. The mortality is high; of 106 cases collected by Thomas, 43 died.

Treatment.—This is surgical; the best incision being that of Delorme, over the submaxillary gland and parallel with the lower jaw.

[1] *Province méd.*, vol. **21**, 6.

CHAPTER VII

DISEASES OF THE ŒSOPHAGUS

By CHEVALIER JACKSON, M.D., D.Sc.,
AND
LOUIS H. CLERF, M.D.

Descriptive.—In the consideration of diseases of the œsophagus it is essential to remember that anatomically it is a long, loose, resilient, redundant, movable tube, fixed in position only at the hypopharynx and at the diaphragm. Between these points it occupies whatever space may be allowed it by surrounding viscera; and this allowance is chiefly during the passage of food or a flow of liquid. Between times it is collapsed with the anterior wall against the posterior wall. Through this collapsed tube there is a continuous, unnoticed trickle of saliva amounting in the aggregate to a few hundred cubic centimeters daily.

Diagnosis.—A list of conditions producing œsophageal symptoms and signs will be found useful for exclusion in diagnosis. Such a list is here given and for the sake of completeness and convenience no attempt is made to avoid overlapping or duplication.

1. Anomaly.
2. Œsophagitis, acute.
3. Œsophagitis, chronic.
4. Erosion.
5. Ulceration.
6. Trauma.
7. Stricture, congenital.
8. Stricture, spasmodic.
9. Stricture, inflammatory.
10. Stricture, cicatricial.
11. Dilatation, local.
12. Dilatation, diffuse.
13. Phrenospasm (cardiospasm).
14. Diverticulum.
15. Compression stenosis.
16. Mediastinal tumor.
17. Mediastinal abscess.
18. Mediastinal glandular mass.
19. Aneurism.
20. Malignant neoplasm.
21. Benign neoplasm.
22. Tuberculosis.
23. Syphilis.
24. Actinomycosis.
25. Varix.
26. Angioneurotic œdema.
27. Hysteria.
28. Paralysis.
29. Foreign body, (*a*) pharynx, (*b*) larynx, (*c*) trachea, (*d*) œsophagus.
30. Antiperistalsis.

Obviously, the exclusion of most of these conditions is largely a matter of general medical and surgical diagnosis. There are, however, two objective diagnostic methods which should be used in practically all cases, namely the roentgen-ray examination and œsophagoscopy.

The Roentgen-ray examination consists of fluoroscopy and radiography, first without a radiopaque mixture to assist in the determination of visceral

disease; then with a swallowed opaque mixture to outline the walls of the œsophagus. If no stenosis is present it is then advisable to have the patient swallow a capsule filled with bismuth subcarbonate or barium sulphate. If the capsule sticks it is suggestive of obstruction; if it be not washed down by a swallow of water, obstruction by a foreign body or by disease may be suspected. If the capsule goes through promptly, œsophagoscopy should be done anyway if there are œsophageal symptoms; it becomes imperative, whether symptoms are present or not, if the capsule lodges even for a short time.

Œsophagoscopy is the diagnostic method of choice, affording all the certainty of objective information and histological examination of any removed specimen of tissue. *This procedure is indicated in any case of abnormality of the swallowing function.* The trained œsophagoscopist can explore the œsophagus without any anesthesia, general or local, in a few minutes, without danger and with a discomfort that does not amount to actual pain. The technique is readily acquired by competent instruction and practically all large medical centres have men well trained in the work.

The blind passage of a bougie is dangerous and inconclusive. All that it can reveal is obstruction; the nature of the obstruction depends on inference, with all the elements of associated error. Moreover the diagnosis is often necessarily made late because the early stages of cancer are not obstructive. Various other diseases as peptic ulcer or other ulceration, œsophagitis, tuberculosis, benign tumors and the like are not obstructive.

In taking the *history* of the patient the utmost care is necessary to avoid being misled by it. For instance, patients come in asserting positively and truthfully that they never had any difficulty in swallowing until two weeks previously; yet the passage of the œsophagoscope has shown a cancer of the œsophagus obviously of many months' growth. On the other hand, other patients come with a history of difficulty in swallowing of twenty years' duration, yet the œsophagoscope reveals a cancer which could not have been present more than a year.

All diseases of the œsophagus manifest themselves sooner or later by the common symptom of difficulty in swallowing—dysphagia. Preceding this, patients often complain of indefinite subjective sensations which cannot be described or localized except in a very vague manner, and as a result they are considered as hysterical or neurotic. Because of this tendency, the diagnosis of œsophageal disease, notably cancer, is often made late.

CONGENITAL MALFORMATIONS

Anomalies of the œsophagus are probably more common than heretofore supposed. Because of the common embryonic origin of the œsophagus and pharynx the trachea is often involved in the developmental error by the formation of an œsophago-tracheal fistula. In some of these the upper and lower segments of the œsophagus open separately into the trachea so that all swallowed fluids enter the air passages.

Congenital webs are not uncommon and are usually found in the upper third of the œsophagus. The diagnosis is made by roentgen-ray study and œsophagoscopy.

Congenital stricture of the œsophagus viewed œsophagoscopically shows a moderate degree of organic stenosis which does not appear cicatricial in character or due to compression. In the absence of a history of swallowing caustics in childhood it must be considered as congenital in origin.

Imperforate Œsophagus.—The common site of atresia is in the mediastinal œsophagus. The upper segment terminates in a more or less dilated, blind pouch. The lower segment may open into the stomach, the central part existing as a cord. The diagnosis is made by fluoroscopic study of the swallowing function and œsophagoscopy. In these cases it has been shown by roentgen-ray study that there is no air in the stomach and intestines.

Congenital diverticulum of the œsophagus has been observed.

Treatment.—Congenital webs are readily cured by œsophagoscopic bouginage. In difficult cases gastrostomy with subsequent retrograde bouginage with the Tucker bougie may be necessary. In cases of imperforate œsophagus there is usually delay in diagnosis because of failure of early recognition of the regurgitation. Early gastrostomy should be done. Removal of salivary secretion by aspiration assists in preventing pulmonary complications. Œsophago-tracheal fistula with an incomplete œsophagus is a hopeless condition. Congenital diverticulum of the œsophagus is amenable to surgical treatment as in adults. Authorities advise waiting until after the second year before operating.

INFLAMMATION OF THE ŒSOPHAGUS

Acute Œsophagitis.—Etiology.—The most common causes are trauma and chemical irritants. It may occur by extension of disease from the mouth and pharynx as in thrush and acute stomatitis, from the stomach in acute gastritis, or the so-called "bilious vomiting;" inflammation of mediastinal structures or of peri-œsophageal tissues may extend to the œsophagus. It may complicate various acute diseases as typhoid fever, scarlet fever, diphtheria, variola and measles; it may occur during pregnancy and is sometimes seen in hookworm disease.

Traumatic œsophagitis may result from the mechanical irritation of a foreign body but far more often follows blind instrumentation to remove a foreign body or for diagnostic purposes. All corrosives, caustics, chemical irritants and hot liquids have a caustic effect. By far the most common of these is *household lye* which contains caustic soda in large amounts. This is obtained from the grocer in packages which may or may not indicate that the contents are poisonous. As a result these substances are carelessly permitted to remain in the kitchen within easy reach of little children who are most often the victims of accidental lye poisoning.

Pathology.—Many degrees of inflammation, varying from simple catarrhal to extensive gangrenous or necrotic œsophagitis, are recognized.

In the simple catarrhal form there is moderate mucosal injection with increased secretion and later epithelial desquamation. In œsophagitis resulting from the ingestion of mild irritants there may be extensive destruction of the epithelium only, which, when desquamating, leaves an intact membrane beneath. Ordinarily, however, chemical irritants, notably lye, produce very severe burns which extend well into the submucosa or areolar coat and are accompanied by extensive necrosis and sloughing so that the mucosa and a part of the submucosa are cast off and may be shed as a membrane.

Symptoms.—These depend largely on the degree of œsophageal involvement. In the milder cases there may be slight distress on swallowing solid foods. When caustics have been swallowed there are marked dysphagia, painful swallowing and substernal pain. There is moderate fever. Because of the severe pain on swallowing and the dysphagia, saliva is expectorated or drools from the mouth. With this there are often associated lung symptoms due to overflow of saliva into the larynx, especially when the patient is asleep. Evidences of water deprivation are usually noted. Palpation of the cervical œsophagus may elicit tenderness.

Sequelæ.—Severe degrees of inflammation with ulceration are always followed by cicatricial stenosis.

Diagnosis.—The history is important if chemical irritants have been swallowed. Occurring during the course of a severe disease, œsophagitis is often not suspected. A positive diagnosis can be made by direct œsophagoscopic inspection.

Prognosis.—In cases of extensive burns death often occurs early from shock, sloughing and perforation. In less severe cases the outlook is hopeful if sufficient fluid and food can be supplied.

Treatment.—The indications are to place the œsophagus at rest and supply the patient with sufficient fluids. The milder forms subside under a regimen of non-irritating liquids and bismuth subnitrate dry on the tongue. Bismuth exerts a protective influence as well as a slight antiseptic action which can be increased by the addition of calomel in small amounts. The addition of anesthesin will do much toward relieving pain on swallowing.

In the severer forms, the caustic cases, sterile water in small quantities should be given by mouth or ice may be sucked. All instrumentation is contraindicated. Sufficient fluids may be supplied by the bowel. Since nutrient enemata are inefficient, gastrostomy should be done if the œsophageal injury is at all extensive.

Chronic Œsophagitis.—This condition is commonly seen in those diseases of the œsophagus which are characterized by stagnation of food, such as diverticulum, stenosis and dilatation. It is also found in drunkards, in heavy smokers or those chewing tobacco and may be associated with a chronic gastritis or pharyngitis. In long-standing cases erosions with ulceration may result.

Symptoms. Although a sense of uneasiness on swallowing may be complained of, there usually are no distinctive symptoms apart from the original condition producing the œsophagitis. Discomfort back of the

sternum or pain extending through to the back is present in some cases. Discomfort after eating may be noticed, if there is retention. These symptoms are insufficient for a diagnosis but they are urgent indications for œsophagoscopy.

Treatment.—In those forms resulting from the frequent swallowing of irritants such as alcohol, hot foods and tobacco, removal of the cause is necessary. Bismuth subnitrate and calomel, dry on the tongue, and the local endoscopic application of argyrol in 20 per cent. solution or silver nitrate in 5 per cent. solution are valuable. Conditions producing food stasis should be corrected. If these cannot be completely cured œsophageal lavage combined with local remedies will assist in limiting the inflammation.

Ulcers of the Œsophagus.—Ulceration is very commonly found in those cases of extensive acute œsophagitis resulting from the ingestion of lye or other caustics; it is also very frequently seen in œsophageal stenosis associated with food stagnation. In chronic œsophagitis, superficial erosions are quite common; these serve to increase the stenosis, whether due primarily to œsophagitis or not and constitute the "vicious circle" described by Chevalier Jackson. Erosions or ulcers may follow from trauma of a foreign body or from instrumentation. Other causes are syphilis, malignant disease, tuberculosis and the chronic infective granulomata. Ulcers may form during the course of long-continued fevers or severe infections of a toxic nature. These are due to digestion of the œsophagus, more commonly the lower end, and are often found in uremia or result from pressure on the œsophageal walls by the cricoid cartilage as in typhoid fever. The last constitutes the so-called decubitus ulcer. Aneurism or other mass may produce a similar condition by compression from without. Peptic ulcer occurring at the lower end of the œsophagus and producing symptoms not unlike those of ulcer of the stomach is occasionally seen.

Symptoms.—The common complaints are substernal pain and difficulty in swallowing. The substernal pain is often referred to the level of the ensiform cartilage, especially in men, and is very probably due to a spastic stenosis although it may be organic. Some patients speak of "pain around the heart." In women the spastic stenosis is usually at the cricoid level and regurgitation of food is immediate. Occasionally there is hematemesis. Secondary infection is often accompanied by fever. Traumatic ulceration may be associated with emphysema and if the cervical portion of the œsophagus is involved, there is tenderness on palpation. Ulceration in typhoid fever often produces no symptoms.

Diagnosis.—The history is of importance. A majority of ulcers occurring in adults are malignant in character. Tuberculous ulceration is usually secondary. In syphilis the Wassermann reaction and therapeutic test are of value. Roentgen-ray study of the chest and of the swallowing function with œsophagoscopy and biopsy will give a correct diagnosis in practically every case.

Prognosis.—This depends on the causative factors.

Treatment.—In simple ulceration the measures outlined under acute œsophagitis, namely, rest of the œsophagus, regulation of diet, local

medication and local endoscopic application will be found useful. Gastrostomy should be done when required. The underlying cause should be treated. Alkalies are indicated to relieve the pain in peptic ulcers. They should also be given in prolonged exhausting diseases or toxic states as a prophylactic. If cicatricial stenosis results, dilatation must be employed.

RUPTURE AND TRAUMA OF THE ŒSOPHAGUS

Spontaneous rupture of the œsophagus is of rare occurrence and probably always is preceded by degeneration or digestion of the œsophageal wall. Trauma, with or without perforation or rupture of the œsophageal wall is most commonly inflicted by instrumentation or by a foreign body. The injury from a foreign body itself is usually slight, does not penetrate deeply and heals promptly. Blind methods of removal, however, are not infrequently attended with serious and fatal trauma.

Symptoms.—The symptoms of slight trauma are similar to those described under acute œsophagitis. Rupture or perforation of the œsophagus is attended by profound shock and collapse. In cases not rapidly fatal, mediastinal emphysema occurs. If the pleura has been perforated a pyopneumothorax will develop.

Treatment.—Treatment of shock and complete rest of the œsophagus with gastrostomy are indicated. If a pyopneumothorax is present thoracotomy should be done. These cases usually prove fatal.

INFECTIVE GRANULOMATA OF THE ŒSOPHAGUS

Tuberculosis.—Tuberculous disease of the œsophagus, although relatively uncommon, probably occurs more often than is generally believed. Painful and difficult swallowing in tuberculosis is always considered to be due to secondary laryngeal involvement and the œsophagus is not investigated. The disease commonly occurs as an extension from a tuberculous process in the larynx, bronchi, pleura, peribronchial lymph nodes and occasionally the lungs or the vertebræ. It may appear as a simple erosion or superficial ulceration, as an extensive ulcerative process in conjunction with the breaking down of peribronchial glands, as a compressive stenosis, a cicatricial stenosis or as a traction diverticulum. The senior author has reported an œsophago-bronchial fistula.[1]

Symptoms.—There is no distinctive group of symptoms which indicates œsophageal involvement. Difficult and painful swallowing may be present. If the larynx is uninvolved there is usually no pain on swallowing.

Diagnosis.—This is made by œsophagoscopy and biopsy in conjunction with the other routine laboratory tests and clinical findings.

Treatment.—Local treatment is ineffective. The œsophagus should be put at rest. Gastrostomy should be done to permit of adequate feeding so that the patient's general resistance may be maintained. The use of a feeding tube is dangerous if ulceration is present. A general anti-

[1] Jackson, Chevalier: *Peroral Endoscopy and Laryngeal Surgery*, 1914, p. 564.

tuberculous regime should be instituted. Pain, if present, may be relieved by the use of orthoform, dry on the tongue.

Syphilis.—Syphilitic involvement of the œsophagus is uncommon and may occur as a mucous patch, an ulcer, a gumma or a cicatricial stenosis. The only symptom usually present is difficulty in swallowing.

Diagnosis.—The œsophagoscopic appearances are not characteristic but must be taken in conjunction with the history, the concomitant lesions, the serological test, the therapeutic test and the examination of tissue. Cicatricial stenosis, occurring late in life, in the absence of any history of swallowing caustics, is suggestive of syphilis.

Treatment.—This consists of anti-syphilitic measures combined with bouginage to prevent the formation of a stenosis while healing. When once established the stenosis yields to bouginage but there is a marked tendency to recurrence. If the dysphagia is marked gastrostomy should be done early.

Actinomycosis.—Actinomycosis and blastomycosis of the œsophagus have been observed postmortem. These should be borne in mind in the histological diagnosis of œsophageal specimens. Trichinosis of the œsophagus also occurs.

VARIX OF THE ŒSOPHAGUS

Because of the absence of symptoms this condition is usually not suspected until there is a spontaneous hemorrhage. The blood which is regurgitated is bright red, not of the "coffee ground" character of vomited blood. Varicosities at the lower end of the œsophagus have been observed in cirrhosis and cancer of the liver.

ANGIONEUROTIC ŒDEMA OF THE ŒSOPHAGUS

Although of rare occurrence this may produce dysphagia which is transitory and is usually associated with vasomotor disturbances elsewhere. The diagnosis can be made only by œsophagoscopy.

Treatment.—This should be directed toward the underlying condition. Temporary tube feeding may become necessary.

HERPES OF THE ŒSOPHAGUS

An authentic case of herpetic eruption involving the œsophagus has been described. Pemphigus also has been observed. These conditions, although curiosities, should be borne in mind as diagnostic possibilities. The diagnosis can be made only with the œsophagoscope.

PARALYSIS OF THE ŒSOPHAGUS

The act of deglutition being purely a muscular process, is dependent on coördinated muscular activity unaided by gravity. To function properly, normal motor and sensory reflex arcs must be present. Any disturbance in either of these will seriously interfere with swallowing or with œsophageal drainage. Paralysis of the œsophagus may be motor or sensory.

Etiology.—The causes of œsophageal paralysis may be grouped under four heads. (1) The toxic type, such as occurs in diphtheria. (2) Functional paralysis which is seen in hysteria. (3) Peripheral paralysis resulting from neuritis. (4) The central or bulbar form, as occurs in glosso-labio-pharyngeal paralysis. *Syphilis* may produce a peripheral or central paralysis. Paralysis may also occur in *myasthenia gravis*, in *poliomyelitis* and has been found associated with the *syndrome of Avellis*. Almost all cases are due to bulbar involvement.

Symptoms.—The only symptom referable to the œsophagus is difficulty in swallowing or inability to swallow. Neither food nor fluid will pass down by gravity; therefore the pyriform sinuses will be seen on indirect mirror examination to be filled with fluid (Chevalier Jackson's sign of œsophageal stenosis). This often overflows into the larynx and produces symptoms referable to the air passages.

Diagnosis.—There is an ever present tendency to mistake œsophageal paralysis for hysteria. Paralysis of the œsophagus is practically always associated with other paralyses about the upper food and air passages which are usually easily recognized if looked for. A history of recent diphtheria is suggestive. A diagnostic œsophagoscopy should be done. In motor paralysis the spasm of the cricopharyngeus is either feeble or absent and there is flaccidity of the œsophageal wall. If there is paralysis of sensation, the reflexes of gagging, coughing and vomiting are lacking.

Treatment.—Œsophagoscopic treatment is of no avail except to assist in the introduction of the feeding tube. The use of the feeding tube is indicated in the absence of erosions or ulceration of the œsophagus. If these are present gastrostomy should be done. Treatment of the underlying cause is a matter for the neurologist and internist.

DILATATION OF THE ŒSOPHAGUS

Diffuse dilatation of the œsophagus is that form of widening of the œsophageal lumen which is commonly found above a stenosis of long standing. The normal œsophagus with its thin weak walls supported by the peri-œsophageal structures is not constituted to act as a reservoir. On the contrary, it is intolerant of the presence of anything except its own secretions and these in small amounts. In the event that there is a stenosis of the lumen sufficient to interfere with the free passage of food or fluids, these accumulate and the œsophagus acts as the reservoir of a large funnel with a small opening through which the contents slowly trickle. This accumulation of food and fluid provides a dilating force which, combined with the influences of stagnation and fermentation of the retained contents, the chronic œsophagitis and erosions, produces a dilatation of the œsophagus, which curiously, always remains when once it has been established (Myer). A certain amount of dilatation is seen in practically every case of long-standing stenosis of the œsophagus. In malignant disease the stenosis does not exist long enough to permit of a very large dilatation. Cicatricial stenosis does not always result in large dilatation probably because of leakage shortening the duration of stasis. Very large dilatations are found in spastic stenosis and in phrenospasm.

The so-called *idiopathic dilatation* of the œsophagus, originally considered a primary disease associated with atonic degeneration of the œsophageal wall, is now believed to be secondary to phrenospasm, so-called cardiospasm. In these cases the underlying cause has often disappeared spontaneously or by treatment and the enormously dilated œsophagus remains.

Diagnosis.—The diagnosis of dilatation of the œsophagus can be made by roentgen-ray study and œsophagoscopy. The large dilatations may simulate a hernia of the stomach but the differentiation can be made by the œsophagoscopist.

Treatment.—This should be directed to correcting the stenosis, relieving the stasis and treating the œsophagitis as indicated under chronic œsophagitis.

PHRENOSPASM (CARDIOSPASM[1])

Cardiospasm, hiatal œsophagismus, functional hiatal stenosis, phrenospasm or preventriculosis, may be described as a symptom-group rather than a distinct disease entity, Numerous designations have been suggested to describe the condition. Although cardiospasm is the more generally used term, it has been demonstrated œsophagoscopically that the stenosis is not at the cardia (Jackson) and by anatomical, clinical and roentgen-ray study that it is not a spasm (Mosher). Since it is not at the cardia and not often if ever truly spasmodic the term "cardiospasm" is a misnomer. The senior author has suggested the term *preventriculosis* and also *ingluviosis* since the condition simulates the normal ingluvies of birds. It is characterized by extensive dilatation of the thoracic œsophagus with marked chronic œsophagitis, and retention of a large quantity of food.

Etiology.—The underlying primary condition is believed by some to be a neurosis. Mosher demonstrated that the abdominal œsophagus, lying in the liver groove or tunnel, may be subjected to a compression stenosis as a result of disease of the left lobe of the liver or of adjacent viscera above or below the diaphragm. Disease of abdominal organs as appendicitis, gall-bladder disease, etc., are regarded as factors by some; others consider endocrine disturbances as contributory (McNab).

It is generally accepted, as originally suggested by Jackson, that the "pinchcock" action of the diaphragm and the kinking of the abdominal œsophagus normally prevent regurgitation when a man with a full stomach is inverted. The senior author believes that this so-called spasm is really a failure of the "pinchcock" to open on the approach of food in the normal cycle of swallowing; in other words that there is a dissociation of the normal reflex mechanism of swallowing. He also suggests the possibility of atavistic activity of ancient nerve paths.

Although a majority of the cases under treatment are adults it will be

[1] There is an interesting difference in the discussion of "cardiospasm" in this section and in that dealing with the Functional Diseases of the Stomach. My understanding of the views of Dr. Jackson and Dr. Clerf on this subject is that in all the patients complaining of "cardiospasm" studied by them, the obstruction has been at the point where the œsophagus passes through the diaphragm, and not at the cardiac orifice of the stomach. EDITOR.

found that in some patients there has been difficulty in swallowing since childhood. This suggests a congenital factor in the etiology.

Pathology.—The typical picture is that of a large diffuse dilatation of the œsophagus either spindle-shaped, which is widest at its middle, or with the most extreme dilatation in its lowest part. The interior is wrinkled, grayish-white and pasty, simulating a furred tongue. Erosions may be present. There is no evidence of new growth or infiltration and the hiatus œsophageus is not stenotic.

Fig. 27

Radiograph of a case of preventriculosis or functional hiatal stenosis (so-called cardiospasm) showing extensive dilatation of the œsophagus.

Symptoms.—The symptoms most commonly noted are a sense of fulness or discomfort referable to the mediastinum, foul breath, an unpleasant taste with frequent expectoration and eructations of gas and the regurgitation of stale food. Regurgitation may occur repeatedly while eating, it may not occur until several hours after or it may be deferred until the patient assumes the recumbent position. The regurgitated food is sour smelling and stale and is found to lack hydrochloric acid, rennin and pepsin. The quantity may exceed several pints and occasionally particles of food are identified which were eaten several days previously.

The vague discomfort is often relieved by regurgitation and is often taken advantage of by the patients. Actual *pain* usually does not occur; when present it is often quite severe. The nutrition is often impaired and occasionally serious inanition exists. Recession of symptoms may occur and this probably accounts for the so-called idiopathic dilatation of the œsophagus unassociated with symptoms.

Diagnosis.—The diagnosis of phrenospasm requires the exclusion of organic disease of the œsophagus. With the fluoroscope and roentgenogram a correct diagnosis can usually be made (Fig. 27). Œsophagoscopy should be done to confirm the diagnosis and to exclude organic disease, especially malignancy. The typical endoscopic appearances are those of a widely dilated œsophagus, with marked static œsophagitis. The hiatus œsophageus is normally contracted and when found will permit a large œsophagoscope to pass. The presence of malignancy, infiltration or cicatricial stenosis at the hiatus would indicate that the static œsophagitis and dilatation were probably the result of organic disease.

Prognosis.—In untreated cases, spontaneous cures are exceptional. Under proper treatment a normal functional result is obtained in a majority of the cases but relapses occur.

Treatment.—The most satisfactory results are obtained by the over-dilatation of the hiatus œsophageus or "diaphragmatic pinchcock" and the carrying out of proper measures for removal of the underlying cause if demonstrable. Careful regulation of diet, œsophageal lavage, bismuth subnitrate dry on the tongue and the internal administration of some preparation of belladonna for the relaxation of spasm seem to benefit some patients.

Occasionally the simple passage of the œsophagoscope will cure; however, more often over-dilatation of the hiatus œsophageus is required. This can be accomplished by the use of Plummer's water bag, with or without a string guide or by Mosher's divulsor placed by endoscopic guidance. The endoscopic placement of a stomach tube or the performance of gastrostomy for feeding to improve nutrition are rarely necessary since there is usually remarkable improvement following the first dilatation.

After a cure has been effected the patient should be instructed regarding the proper selection and mastication of foods. Coarse fibrous foods should be avoided.

DIVERTICULUM OF THE ŒSOPHAGUS

Diverticula of the œsophagus are classified according to their etiology as traction and pulsion forms. In the *traction* form the coats of the œsophagus are all represented in the wall of the sac, while in the *pulsion* variety the muscular coat is partially or completely absent. The orifice of the subdiverticular œsophagus in a traction diverticulum is devoid of any normal constriction while in the pulsion form the subdiverticular orifice is constricted by a normal sphincter, the cricopharyngeus. The senior author believes that the absence of this muscular constriction in traction

diverticula accounts for the non-retention of food in these cases while the reverse holds true in pulsion diverticula.

Traction Diverticulum.—Traction diverticulum of the œsophagus usually occurs in the thorax. It rarely produces symptoms and is more often accidentally observed by the roentgenologist in the course of a routine examination of the gastro-intestinal tract. It is supposed to result from traction, during cough, swallowing and respiration, on localized adhesions between the œsophagus and peri-œsophageal structures, such as peribronchial lymph glands. Since the orifice is lower than the fundus the sac empties itself readily, there is no stasis and symptoms are uncommon; occasionally, however, a case is seen in which there is dysphagia resulting from cicatricial stenosis of the subdiverticular œsophagus. This usually responds readily to œsophagoscopic bouginage.

Pulsion Diverticulum.—Pulsion diverticulum of the œsophagus, primarily small, may remain so or may increase to an enormous size.

Etiology.—A pulsion diverticulum is essentially a hernial protrusion of the œsophageal mucosa occurring between the oblique and circular fibres of the inferior constrictor muscle of the pharynx. Chevalier Jackson calls attention to the action of the latter group of fibres as constituting the "cricopharyngeal pinchcock," which is always closed except when it momentarily opens at the approach of the bolus in normal swallowing. Failure to open promptly puts an enormous and undue strain on the weak point in the support of the hypopharyngeal wall, through which the wall herniates in consequence. This dissociation of reflexes he regards as the chief *active* etiological factor. The *passive* factors are the embryological and anatomical fundamentals demonstrated by Mosher[1] who believes that asymmetry of the mouth of the œsophagus and congenital webs may be a factor in the mechanism of the pouch formation. Pulsion diverticulum usually occurs after the fiftieth year of life and is more common in men than in women. Hasty eating with improper mastication of food, defective teeth, swallowing too large a bolus and spasm of the upper œsophageal orifice are contributory factors.

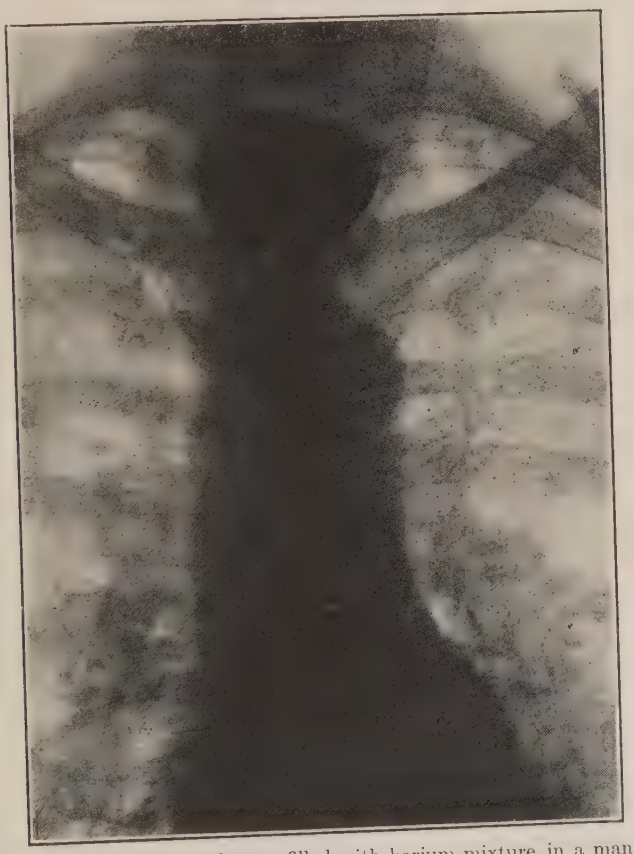
Pathology.—With a triangular-shaped weak point behind the cricoid cartilage between the oblique and the orbicular fibres of the inferior constrictor muscle of the pharynx, the orifice of the diverticulum is usually near the mid-line. As the sac enlarges its bulk is displaced to one side, more often the left. Since the pouch fills before food can pass down the œsophagus the subdiverticular œsophagus is compressed by the distended pouch increasing the stenosis, which in turn produces greater distention of the sac constituting a "vicious circle."[2] The natural tendency is toward a steady increase in the size of the pouch so that it may extend into the thorax. With stagnation of food there is a static œsophagitis and in long-standing cases there may be erosions or ulceration, with a variable degree of cicatricial stenosis about the orifice of the subdiverticular œsophagus. Malignant disease is an occasional secondary development.

[1] Asymmetry of the Mouth of the Œsophagus and Retropharyngeal Diverticulum, *The Laryngoscope*, 1924, **34**, 854.

[2] Jackson, Chevalier: *Peroral Endoscopy and Laryngeal Surgery*, 1914.

Symptoms.—A subjective sensation on swallowing, regurgitation of minute quantities of food and an annoying, hawking cough are among the earlier symptoms noted. Later, the swallowing becomes more difficult, regurgitation is more frequent, there is a gurgling sound noted on swallowing, the breath possesses a peculiar, stale or foul odor and nutrition becomes impaired. A large diverticulum when filled may interfere with breathing. Often there is frequent coughing on lying down because of overflow of secretion into the larynx. On mirror examination a moderate degree of laryngo-tracheitis will be found. In long-standing cases there is often a chronic bronchitis.

FIG. 28



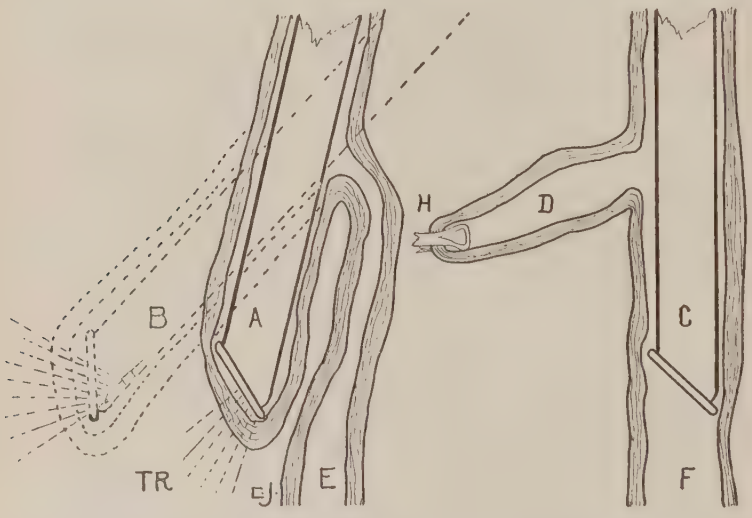
Pulsion diverticulum of the œsophagus, filled with barium mixture, in a man, aged sixty-five years. The diverticulum was afterward removed by the Gaub-Jackson method.

Diagnosis.—A tentative diagnosis of diverticulum can be made from the symptoms and the Boyce and Clerf signs. The patient is asked to swallow, which puts air in the diverticulum. Pressure with the fingers low on the neck will force out the air and cause a gurgling sound heard at the patient's open mouth (Boyce sign). If, by indirect mirror laryngoscopy, the laryngeal mirror be watched bubbles will be seen to emerge

from one or other pyriform sinus (Clerf sign). Roentgen-ray study with an opaque mixture, preferably bismuth, is the first step in making a positive diagnosis (Fig. 28). Œsophagoscopy should always be done to confirm the diagnosis and especially to exclude malignant disease and cicatricial, compressive or spasmodic stenosis. Aneurism should always be excluded by physical examination and fluoroscopic studies. Blind bouginage gives no conclusive information and is an extremely dangerous procedure.

Prognosis.—In untreated cases, there is usually a progressive increase in the size of the sac because of the "vicious circle," with a consequent increase in symptoms. Recurrence after operation is occasionally seen.

FIG. 29



Schematic representation of œsophagoscopic aid in the excision of a diverticulum in the Gaub-Jackson operation. At *A* the œsophagoscope is represented in the bottom of the pouch after the surgeon has cut down to where he can feel the œsophagoscope. Then the œsophagoscopist causes the pouch to protrude as shown by the dotted line at *B*. After the surgeon has dissected the sac entirely loose from its surroundings, traction is made upon the sac as shown at *H* and the œsophagoscope is inserted down the lumen of the œsophagus as shown at *C*. The œsophagoscope now occupies the lumen which the patient will need for swallowing. It only remains for the surgeon to remove the redundancy without risk of removing any of the normal wall. (From Bronchoscopy and Œsophagoscopy by Chevalier Jackson, W. B. Saunders Co.)

Treatment.—The best results in the treatment of pulsion diverticulum are obtained by the combined internal and external operation—the Gaub-Jackson method—performed in one or two stages (Fig. 29). Mosher advocated cutting the common wall between the sac and œsophagus with scissors through the œsophagoscope. Other methods of treatment of the sac have been devised. Œsophagoscopic dilatation of the orifice of the subdiverticular œsophagus may be resorted to in a small pouch with good prospect of at least temporary relief. Palliative treatment, consisting of frequent lavage of the sac should be used if operation is contraindicated by organic disease elsewhere. Lavage should be carried out by the patient after each meal. It consists in first filling the sac by

swallowing water; the head and neck are then lowered and with slight pressure made over the root of the neck, corresponding to the fundus of the sac, its contents are evacuated through the open mouth.

NON-MALIGNANT STENOSIS AND STRICTURE OF THE ŒSOPHAGUS

Œsophageal obstruction of this nature may be spasmodic, compressive or cicatricial in character.

Spasmodic Stenosis of the Œsophagus.—The œsophagus is dependent upon reflex action for its normal activity in the propulsion of the bolus of food. Once started, the bolus is carried along by a series of peristaltic waves, reflexly excited, until it reaches the stomach. Any disturbance in the normal reflex arc produced by abnormal stimuli may result in a contraction or spasm of the œsophagus replacing the normal waves and producing obstruction.

This reflex may result from hurried gulping of large boluses of food. A common source is local disease of the œsophagus itself, as superficial erosions, ulcers, chronic œsophagitis, cancer or foreign bodies; in fact any œsophageal disease may excite sufficient spasm to produce obstruction. In addition, œsophageal spasm may be secondary to disease remote from the gullet. Thus, spasm may occur in diseases of the stomach, as cancer, ulcer, and hyperacidity or in diseases of the liver and biliary apparatus. In established cases, an undoubted perpetuating cause is the so-called "nerve cell habit." In these there is a basic neurotic factor and very often the stigmata of hysteria are found. Although occurring at any age œsophageal spasmodic stenosis is uncommon after middle life. Spasm was observed by the senior author in an infant aged two days. Simple dilatation by the œsophagoscope without anesthesia resulted in complete cure. McKinney reports a spasmodic stenosis of the œsophagus in a child aged thirteen months. As pointed out by Chevalier Jackson it should never be forgotten that spasmodic stenosis may be symptomatically simulated by the intermittent obstruction caused by the lodgment and subsequent dislodgment of food in an organic stricture.

Globus hystericus is a term used to designate the sensation described by patients as a "lump rising in the throat when swallowing." Although previously considered as a manifestation of hysteria, it has been demonstrated by œsophagoscopy that often a contraction of the cricopharyngeus is the cause of this sensation. Before reaching a diagnosis of globus hystericus, œsophagoscopy should be done as contraction of the inferior constrictor is often excited reflexly by organic disease of the œsophagus.

Cricopharyngeal spasmodic stenosis, although but occasionally associated with hysteria, is very often erroneously thus diagnosed. It is essentially a spasm of the circular fibres of the inferior constrictor muscle of the pharynx, the cricopharyngeus, and the chief complaint is difficulty in starting the bolus of food downward. Once started, it passes on unimpeded.

Diagnosis.—Having decided by roentgen-ray study that there is stenosis at the level of the cricopharyngeus, œsophagoscopy is indicated to decide whether it is spasmodic, organic or both. Spasmodic stenosis may occur

secondary to an organic stenosis. Spasm may be due to organic disease of any portion of the œsophagus or to disease of remote organs. A patient was recently observed who complained of difficulty in starting the bolus of food. By œsophagoscopy a diagnosis of cancer of the lower end of the œsophagus was made.

Treatment.—This should be directed toward removing the basic source of the morbid reflexes. All of the purely functional cases can be cured of symptoms by the passage of a large œsophagoscope. Relapses are common and require similar treatment at varying intervals.

Compression Stenosis of the Œsophagus.—Stenosis of the œsophagus may be produced by the pressure of any peri-œsophageal disease. It occurs most often in lesions of the intrathoracic viscera. Among the most common are enlargement of the thyroid gland, either cervical or thoracic, aneurism or calcification of the thoracic aorta, cardiac enlargement, mediastinal glandular enlargement, malignancy of any of the intrathoracic organs including the lungs and pleura, and deformity of the spine. The most common symptom is dysphagia. Involvement of the recurrent laryngeal nerve in the compressive mass often produces a coëxistent laryngeal paralysis.

Diagnosis.—Although a diagnosis of compression stenosis of the œsophagus can be made by œsophagoscopy, this diagnostic measure should always be preceded by careful physical examination, serological studies, radiography of the chest and fluoroscopic studies of the swallowing function to determine the nature of the compressive lesion. The presence of an aneurism is usually considered a contraindication to œsophagoscopy except for foreign body.

Treatment.—The treatment of compression stenosis depends upon the cause and is usually a problem for the internist or surgeon. Intubation of the œsophagus may be done in all conditions except aneurism. Gastrostomy, if necessary, should be done early. In uncertain cases a thorough course of mercury and iodides should be given as an occasional cure results from their use.

Cicatricial Stricture of the Œsophagus.—This form of stenosis is most commonly the result of the accidental swallowing of corrosive poisons, especially caustic alkalies. These enter very largely into the manufacture of the various lyes, washing powders and cleansers and as such are sold by the grocer. Being improperly or inadequately labelled regarding their poisonous nature, these preparations are placed within the reach of little children, who unfortunately constitute a majority of the cases of lye burns of the œsophagus. Needless to say this is a preventable accident. Other poisons such as strong acids, ammonia, and bichloride of mercury are less frequent causes. Cicatricial stenosis may follow ulceration of the œsophagus occurring as a complication of typhoid fever, scarlet fever, diphtheria, tuberculosis, pyogenic effections, syphilis, prolonged sojourn of a foreign body, trauma by instrumentation and during pregnancy. It may also result from the erosions and ulcerations occurring in chronic œsophagitis. A cicatricial stricture of the œsophagus always takes its origin in any ulceration, inflammation or injury in which there is loss of tissue. The degree of stenosis is dependent in great part upon the extent of the ulcera-

tion and the area of surface involved. In the case of corrosive poisons, the more concentrated they are, the greater will be the tissue destruction and the resulting degree of stenosis.

The most common *site* of stricture is in the middle third of the œsophagus at the crossing of the left bronchus; next in order is the region of the cricopharyngeus; then the hiatal region. Strictures are often multiple, especially in the caustic cases and their lumina are practically never concentrically placed (Fig. 30).

Fig. 30

Roentgenogram showing extensive stenosis of the œsophagus in a child aged three years, from the accidental ingestion of lye ten weeks before admission to the hospital. The œsophagus above the stenosis is greatly dilated.

Symptoms.—The most constant symptom is dysphagia which grows progressively worse. Solid foods are first affected and later liquids are swallowed with difficulty. With the progressive dysphagia there is regurgitation. Loss of weight is variable depending upon the amount of food and fluid that can be swallowed. In marked stenosis there is always emaciation with a variable degree of water starvation which immediately assumes a serious aspect if the stenosis becomes complete. With the

overflow of fluids and saliva into the larynx there is always a laryngotracheitis. As a result of this, bronchopneumonia is a common and serious complication.

Diagnosis.—A history of dysphagia occurring after an œsophageal injury is of vast importance. A positive diagnosis is made by careful roentgen-ray study without and with an opaque mixture and by œsophagoscopy. Blind bouginage, being an inconclusive and extremely dangerous procedure, possesses no diagnostic value.

Prognosis.—Spontaneous cures never occur. In untreated cases of stricture with small lumina the mortality-rate is very high. Blind methods of bouginage are almost certain to result in perforation of the wall of the œsophageal dilatation which always forms above the stenosed lumen. Mortality from œsophagoscopic procedures is slight. With early gastrostomy and modern methods of treatment practically all patients can eventually be cured.

Treatment.—Maintenance of the patient's nutrition is the first consideration. Dilatation of the œsophagus, unless the stenosis is slight, requires a long time if a safe method is used. Gastrostomy should be done early whenever necessary. This allows proper alimentation, puts the œsophagus at complete rest, removes the irritating influences of static œsophagitis and, what is most important, permits the carrying out of very safe and rapid method of treatment, namely continuous string retrograde bouginage with the Tucker bougie.[1] Various other methods of dilatation are employed. Œsophagoscopic bouginage, using graduated flexible-tipped, filiform bougies, is a safe but slow method. Forcible dilatation, by passing a bougie over a string or wire guide or by a special divulsor can be used. Good results have been obtained by electrolysis. Internal œsophagotomy by endoscopic methods or by the string saw are dangerous and questionable procedures. In complete stricture of the œsophagus the cicatricial barrier can be removed by external œsophagoplasty if the stenosis involves the cervical œsophagus. The senior author devised an operation in which, by combined peroral and retrograde œsophagoscopy performed under the guidance of the Manges double-plane fluoroscope, the cicatricial barrier is perforated by special forceps under direct endoscopic guidance. A string is carried through and later dilatation is performed with the Tucker retrograde bougie.

CARCINOMA OF THE ŒSOPHAGUS

Cancer of the œsophagus is among the most important œsophageal diseases because of its frequency. It may be safely stated that a majority of the stenoses of the œsophagus occurring during adult life are malignant in nature.

Etiology.—As in cancer elsewhere, no positive causative factors can be assigned; however, it is assumed that prolonged irritation is a predisposing cause. This would, in part, explain its more common occurrence at the points of anatomical narrowing of the œsophagus, also at the site of

[1] Cicatricial Stenosis of the Œsophagus, *Ann. Otol. Rhinol. and Laryngol.*, 1924, **33**, 1180.

old scars and from traction diverticula. In some cases there is a history of prolonged use of strong alcoholic beverages or the habitual drinking of very hot liquids. Carcinoma of the œsophagus is more common in males than females; it is most frequently seen in middle life, in the late forties and in the fifties.

Pathology.—The most frequent type of cancer is the squamous-celled form. Adenocarcinoma occurs in the lower end of the œsophagus or more commonly involves the œsophagus as a secondary growth by extension from the stomach. Cancer of the œsophagus probably occurs more often in the upper third, the lower third being next in frequency of involvement. It is nearly always a primary growth. Secondary involvement may occur as an extension from a growth at the cardiac end of the stomach, from the thyroid gland, from cancer of the larynx or hypopharynx or rarely from carcinoma of the lungs or pleura.

Although carcinoma may appear as a leukoplakic area, as a submucosal infiltration covered by normal mucosa and associated with bulging of the œsophageal wall, or as polypoid masses, it is more often seen as an area of ulceration projecting but little above the surface or as a large cauliflower fungation which always bleeds very readily when touched. As a rule, the extent of involvement is not great although occasional cases have been observed in which almost the entire length of the gullet was involved. The degree of stenosis is dependent on the size of the growth, the amount of spasm set up by its presence and the reaction resulting from the passage of food and the static œsophagitis. A moderate dilatation is often found above the stenosis.

Symptoms.—In the early stages of œsophageal cancer there often are no symptoms. If present they are described as indefinite sensations which are localized in a vague manner and the patient is often considered to be neurotic. Occasionally there may be an inconstant cricopharyngeal spasmodic stenosis. The most common early symptom is slight difficulty in swallowing solid foods. Too often this is ignored by the patient and he does not consult his physician until he can no longer swallow solid and semi-solid foods. When this occurs there is a progressive loss of weight, the stenosis increases so that an adequate quantity of fluids can no longer be taken and rapid decline from water starvation ensues. Regurgitation of foul, blood-streaked material occurs late in the disease and suggest ulceration with secondary infection. Although *pain* may be an early symptom it more often occurs late in the disease. When present it is deep-seated and of an aching character, and is referred to the back or may be substernal. *Cough* is often present and is due to overflow of secretion into the larynx. Involvement of the recurrent laryngeal nerves may produce unilateral or bilateral paralysis with hoarseness, aphonia, dyspnœa and possibly aspiration pneumonia. Perforation of the œsophagus into the air passages or the pleura, into the mediastinal tissues or even into the pericardium may occur. This is necessarily fatal because of the severe infection which results.

Diagnosis.—Every patient complaining of symptoms referable to the œsophagus should have a careful fluoroscopic study of the swallowing function. Aneurism should be ruled out by a study of the thorax and by

roentgen-ray examination. Syphilis and tuberculosis should be eliminated by suitable tests. Œsophagoscopic examination and the removal of a specimen of tissue for biopsy render the diagnosis certain. Bouginage is inconclusive, dangerous and is to be condemned.

Prognosis.—This is hopeless, the mortality-rate being 100 per cent. Unless patients with œsophageal symptoms can be given the benefit of early diagnostic study with the roentgen-ray and the œsophagoscope, the present mortality-rate will remain unchanged.

Treatment.—This is palliative, being directed toward the relief of the dysphagia to prevent starvation and the ultilizing of such measures as may inhibit the activity of the cancerous process. Practically every patient with œsophageal cancer will die of starvation unless intercurrent disease supervenes. Gastrostomy is always indicated when dysphagia occurs and should be done early before nutrition is greatly impaired. It also serves to remove the irritation produced by decomposing and stagnant food. Intubation of the œsophagus, using the Guisez or the Charters-Symonds intubation tubes, may delay gastrostomy but will not obviate the need for its ultimate performance. These tubes should be changed every week for cleaning, a duplicate tube being immediately reinserted. As the growth progresses smaller tubes are needed until finally none can be inserted. Dilatation of the stenosed lumen by bouginage is associated with great risk of perforating the œsophageal wall. As great a variety as possible in liquid diet should be given: fruit juices and vegetable soups properly strained can be given in addition to milk and eggs.

Radium or roentgen-ray therapy, used separately or in combination, retard the progress of œsophageal cancer. Marked temporary improvement in the swallowing of foods with prolongation of life is often noted. Radium may be applied to the chest wall or be introduced into the œsophagus with the aid of the œsophagoscope or by the string method. Deep roentgen-ray therapy exerts a favorable influence and seems to possess some advantages over radium; however it is a question whether either ever cured cancer of the œsophagus.

The surgical extirpation of œsophageal cancer has met with little success. This is primarily due to the fact that the diagnosis is nearly always made late in the disease when there is marked obstruction with dysphagia and loss of weight. There seems ample justification for the view that when every patient with beginning dysphagia is given the benefits of early roentgen-ray study and œsophagoscopy, surgical extirpation will show a certain percentage of cures, because of the relatively low degree of malignancy of cancer of the œsophagus.[1]

SARCOMA OF THE ŒSOPHAGUS

Primary sarcoma of the œsophagus is of relatively uncommon occurrence (Orton[2]). It occurs more often late in life and usually involves the thoracic œsophagus. It is found more often in males. The symptoms

[1] Jackson, Chevalier: Carcinoma and Sarcoma of the Œsophagus, *Am. Jour. Med. Sci.* 1925, **169**, 625.

[2] Sarcoma of the Œsophagus. *Ann. Otol. Rhinol. and Laryngol.*, 1924, **33**, 1236.

are not unlike those of carcinoma of the œsophagus, the first most commonly noted being difficulty in swallowing solid food. With this there is regurgitation of food, progressive inanition and pain which may be referred to any part of the thorax or to the shoulders and neck. The correct *diagnosis* can be made only by œsophagoscopy and biopsy. The *treatment* is palliative. Gastrostomy should be done early to prevent starvation. Radium and deep roentgen-ray therapy tend to prolong life and also relieve pain.

BENIGN TUMORS OF THE ŒSOPHAGUS

Benign neoplasms of the œsophagus are of rare occurrence. Fibromata, lipomata, myomata, adenomata and papillomata have been reported. Epithelial and dermoid cysts have been observed and in addition cysts resulting from the retention of glandular secretion have been noted. Symptoms of difficulty in swallowing would be manifested only when the tumor assumed sufficient size to produce stenosis. A diagnosis can be made only by roentgen-ray examination and œsophagoscopy with biopsy.

FOREIGN BODIES IN THE ŒSOPHAGUS

Foreign bodies in the œsophagus are almost always introduced from without by way of the natural passages although they may occasionally enter by penetration or may originate from within the body. They are more commonly found in children and in the insane. The majority of foreign bodies consist of substances which are not articles of food and therefore should never have been placed in the mouth. Articles of food make up a small percentage of the cases and usually are insufficiently masticated or cooked; more often, however, articles of food are found obstructing the lumen of an œsophagus which is the seat of previous disease. The objects most frequently found are buttons, coins, and other disks, safety pins, toys, bones, artificial dentures and boluses of food.

The most common site of lodgment of an œsophageal foreign body is in the cervical portion at the level of the suprasternal notch. Although anatomically a constriction cannot be demonstrated at this point, nevertheless there is a physiological narrowing of the œsophagus at this level. This is produced in great part by the crowding together of the viscera into the narrow, rigid upper thoracic aperture.

Symptoms.— *Dysphagia* is the most common complaint in œsophageal foreign body. This difficulty may be so slight as to produce little or no discomfort or there may be aphagia. Tilting or shifting of a foreign body may produce intermittent dysphagia or even aphagia. Regurgitation of food or secretion may occur if the obstruction is marked. *Pain* is an inconstant symptom and when present is usually caused by penetration of a pointed object, by secondary inflammation or by impaction of a large foreign body. A subjective sensation of a foreign body is usually complained of but this cannot be depended on as a localizing sign since it often persists for a time after the removal of or the passage onward of the object. A sticking sensation can often be elicited in pointed foreign bodies in the cervical œsophagus by pressure on the trachea at a point

opposite the site of lodgment of the foreign body.[1] Cough associated with the physical signs of a tracheo-bronchitis may result from overflow of secretions into the larynx, or perforation, either ulcerative or traumatic, of the posterior tracheal wall permitting leakage of secretion or food into the trachea. Dyspnœa may be produced by a large object compressing the larynx or trachea.

Diagnosis.—Every patient who complains of something having stuck in his throat after swallowing should be regarded as a foreign body case until every means of diagnosis has been utilized. A definite routine examination should be followed and should include the history, complete

FIG. 31

Radiograph showing a coin (nickel) in the œsophagus of a child, aged two years Coins or other disks lodged in the œsophagus are found with their greatest diameter in the coronal plane. This serves to distinguish them from tracheal foreign bodies since these lie with their greatest diameter in the sagittal plane. In addition, the tracheal shadow can be distinctly seen in front of the coin. Coin removed by œsophagoscopy without anesthesia general or local.

physical examination, roentgen-ray studies and œsophagoscopy. A careful history should be taken noting the details of the accident, initial symptoms and the subsequent development of signs or additional symptoms. A complete general physical examination should be made including a careful inspection of the nose, mouth, throat, larynx and pyriform sinuses; studies also should determine the presence of aneurism, cardiac disease, hypertension, disease of the central nervous system or any other condition which might render œsophagoscopy hazardous. The presence

[1] Tucker, G.: Retropharyngeal Abscess from Lodgment of Foreign Body in the Œsophagus, *Jour. Am. Med. Assn.*, 1925, **84**, 54.

of cellulitis, emphysema of the neck or signs of mediastinitis should be ascertained.

Roentgen-ray studies should be made in every case of suspected foreign body. In all cases of radiopaque foreign body, antero-posterior and lateral roentgenograms should be made (Fig. 31). The location of non-opaque objects (such as small bones, buttons, etc.), can be determined

FIG. 32

Roentgenogram showing a bismuth-filled capsule lodged in the cervical œsophagus of a man, aged forty-nine years, who developed dysphagia immediately after choking while eating chicken. Fluoroscopic examination, without the aid of an opaque mixture showed no evidence of an œsophageal foreign body. A 00 capsule containing bismuth, when swallowed, lodged at a point immediately above the suprasternal notch and remained there until dissolved. At diagnostic œsophagoscopy there was removed a large triangular shaped bone, from the sternum of a chicken, which was found lying in the coronal plane of the body immediately below the cricopharyngeal fold.

by fluoroscopic study of the swallowing function with a bismuth-filled capsule or bismuth mixture (Fig. 32). In doubtful cases a diagnostic œsophagoscopy should always be done.

Prognosis.—Certain foreign bodies may remain a long time in the œsophagus without producing harmful results; ultimately however ulceration, cellulitis, fistulous tracts and cicatricial stenosis occur. Perforating foreign bodies may rapidly prove fatal from hemorrhage or from

cellulitis and septic mediastinitis. Pressure on the trachea or larynx may produce asphyxia or perichondritis of the tracheal or laryngeal cartilages. Carefully performed œsophagoscopic removal is successful in about 98 per cent. of the cases. Blind methods of removal are dangerous and often produce more trauma than would be caused by the foreign body if permitted to remain undisturbed.

Treatment.—Prophylaxis.—Since carelessness is the most frequent of all causes of foreign bodies in the œsophagus (over 80 per cent. of cases), the question of foreign body prevention offers a fruitful field in the education of the laity.

Œsophagoscopy is successful in the removal of foreign bodies through the mouth in fully 98 per cent. of all cases. This can be done without anesthesia, general or local, and with a discomfort that does not amount to actual pain. It is a highly technical procedure requiring a special instrumentation, organization and training, a detailed consideration of which is not within the scope of this article.

Contraindications to Œsophagoscopy.—There are no contraindications to carefully performed œsophagoscopy for foreign body removal. For other conditions the presence of aneurism, a high degree of hypertension and advanced cardiovascular disease may render it inadvisable. Cellulitis and emphysema of the tissues of the neck, septic mediastinitis and perforation of the œsophagus from previous ill-advised attempts at removal usually call for postponement of the œsophagoscopy until the effects of the trauma have subsided. Treatment as indicated under acute œsophagitis and rupture and trauma of the œsophagus, should be carried out.

CHAPTER VIII

FUNCTIONAL DISEASES OF THE STOMACH

By JULIUS FRIEDENWALD, M.D.

GASTRIC NEUROSES

Introduction.—Gastric neuroses are those functional disturbances of the stomach manifesting symptoms which are not based upon any anatomical pathological changes. A certain number of the so-called gastric neuroses, dependent without question upon some form of anatomical change, have eluded our means of detection. With more exact methods of investigation, the number of gastric neuroses will be lessened in number, and some of these diseases be placed upon a more definite anatomical basis.

It is now but little understood in what manner the disturbances of innervation take place; it is well known, however, that the branches of the vagus and abdominal sympathetic carry the impulses to and from the stomach, and it is through these nerves that these disturbances of innervation occur; while we cannot trace the exact paths, it is generally believed that the impulses of motility, sensation, and secretion are transmitted by different nerves; since any of these disturbances may exist alone and independently of the other, we therefore believe in the existence of special nerves of motion, secretion, and sensation.

It will not be out of place to briefly discuss a few points associated with the nervous mechanism of the stomach. Between the circular and longitudinal muscles there is a plexus of nerves (Auerbach's plexus) by means of which a local nervous mechanism is maintained. Intimate connection with the great nerve centres is had through the vagi, while in addition to these the sympathetic sends fibres to the stomach. It has not yet been entirely determined whether the rhythmic contractions of the stomach and intestines are entirely under nervous control, since this special process is regarded by some as being of muscular origin alone. Magnus considered these contractions of nervous origin. He succeeded in obtaining rhythmic movements of the muscles of the intestines taken from the body which still held the plexus of Auerbach, even after the removal of the plexus of Meissner and the mucosa.

The sympathetic nervous system plays a large part in these functional disturbances. There are two divisions which must be distinguished from each other. The first (thoracico-lumbar), known as the sympathetic proper, supplies the bloodvessels, glands and smooth muscle fibres, including those of the stomach and intestines, bile and pancreatic ducts, liver and pancreas, colon, sigmoid and rectum.

The second (cranio-bulbar and sacral) (parasympathetic), includes the nerves taking their exit from the mid-brain, hind-brain, and sacrum,

supplying the glands and muscles of the gastro-intestinal tract, the œsophagus, stomach, intestines, liver, biliary passages, pancreas and ducts, colon, sigmoid and rectum. This group has been termed "the vagus system in the larger sense."

Through the researches of Eppinger and Hess, the theory has been advanced that disturbances of the sympathetic system leading to increased and decreased tonus or excitability, may be the cause of certain pathological changes, and the activity of the glands of internal secretion influenced. Eppinger and Hess evolved clinical symptom complexes, based on the excitability or tonus of the sympathetic system, which they termed vagotonia and sympatheticotonia. The effect of the increased tonus of the cranio-sacral system controlling the digestive organs consists in an increase in secretion of the stomach glands (hypersecretion and hyperacidity), increased gastric peristalsis (nervous vomiting), cardiospasm, pylorospasm, spastic constipation, increased intestinal peristalsis (nervous diarrhœa), mucous colitis, and spasm of the rectal sphincter.

As forms of increased sympatheticotonia, may be mentioned, atony of the stomach, ptosis, atony of the intestines with increased constipation achylia gastrica, nervous anacidity and relaxation of the anal sphincter.

While certain drugs produce a definite stimulating effect on the vagus, the effect of others is inhibiting. Similarly there are drugs which are sympatheticotonic. The endocrine function is closely related to the sympathetic system, the activity of which is to a degree dependent upon the secretion of the endocrine glands, while on the other hand, the internal secretions are in part controlled by the sympathetic nervous system.

Cannon[1] and others demonstrated that the pylorus is partially under local nervous control for destruction of either of the vagi or the sympathetic system does not prevent the passage of the chyme from the stomach into the intestine. As the stomach is highly autonomous in its action and the mechanism producing peristalsis is found in its wall, Alvarez[2] maintains that this function is seated largely in the muscular structure of the stomach and that Auerbach's plexus simply serves for the conduction of stimuli and the coördination of movements.

There is no question that the sphincters of the stomach are partially controlled by the central nervous system. With special reference to the cardia, Langley[3] showed that the vagus contains both inhibitory and accelerator fibres, while Openchowski[4] demonstrated that stimulation of the sympathetic increases the contraction of the cardia. In reference to the pylorus, May[5] has shown that stimulation of the vagus causes at first an inhibition followed by an acceleration of the contraction of the pylorus. In regard to the nervous mechanism of other portions of the stomach, May demonstrated that stimulation of the vagus caused at first an inhibition of the peristalsis of the pyloric portion, with a lessened tone of the cardia, followed later by an acceleration of peristalsis in the pyloric region with increased tone in the cardia. Carlson[6] noted that hunger contractions are mainly in the fundus, while the digestive con-

[1] *Am. Jour. Physiol.*, 1905, **13**, 22.
[2] *The Mechanics of the Digestive Tract*, p. 6.
[3] *Jour. Physiol.*, 1898, **23**, p. 407.
[4] *Centralblatt für Physiol.*, 1889, S. 1.
[5] *Jour. Physiol.*, 1904, **30**, 400.
[6] *Am. Jour. Physiol.*, 1913, **32**, 245.

tractions are mainly in the pyloric region. Cannon has shown that emotion plays an important role in the movements of the stomach by demonstrating that peristalsis ceases whenever "the animal manifests signs of rage, distress, or even anxiety." According to Cannon the stomach is divided into two parts that are physiologically distinct. The larger part is the cardiac area, the smaller the pyloric. During the process of digestion there are constant peristaltic movements running over the surface of the pylorus. Peristaltic waves are not present in the cardiac area. After the pylorus empties itself, however, the cardiac portion produces a tonic pressure, forcing its contents into the pyloric area; therefore, mixture with the gastric secretion takes place in the pyloric area. The food remains, however, for some time in the cardiac area, during which the salivary digestion is continued. According to Cannon the presence of free hydrochloric acid in the stomach bears an important relation to the relaxation of the pyloric sphincter, causing the pylorus to open and so permit the escape of the acid chyme into the duodenum. The presence of acid in the duodenum produces a reflex stimulation of the pylorus, which closes and remains so until the contents of the duodenum have again become alkaline.

Cannon has shown that mechanical stretching stimulates activity in smooth muscles, and as this form of muscle surrounds the stomach, and intestines (which fill up and then empty), the effect of the distention becomes manifest. Thus when the muscle is in a state of tonus, stretching is followed by a contraction, but when the stomach is atonic, flaccid distention is not followed by contraction. According to Cannon "the view that tonicity of the neuro-musculature of the alimentary canal is a fundamental necessity for the appearance of rhythmical movements harmonizes many diverse observations." It accounts for the lack of motility in atony of the stomach, and gives an explanation for the existence and importance of extrinsic motor nerves. It also explains why worry, anxiety and distress inhibit gastro-intestinal movements, for such conditions accompanied by splanchnic impulses abolish tonus.

The chemical theory of Cannon regarding the control of the pyloric sphincter does not explain such well-established facts as the rapid emptying of the stomach of water or its emptying in achylia gastrica. According to Luckhardt, Philips and Carlson,[1] and McClure, Reynolds and Schwartz[2] certain motor activities of the stomach have a direct bearing upon the relation of the pyloric sphincter, thus indicating the presence of a mechanical as well as a chemical factor associated with this phenomenon. Inhibition of the pyloric sphincter may be induced by increased motor activity as well as by the effect of free hydrochloric acid and thus lead to the relaxation of the pylorus. According to these investigators very soon after the ingestion of food the pylorus relaxes for the passage of food with the appearance of strong waves of contraction at the pylorus, which are increased by the increased muscular tone of the entire stomach.

According to Alvarez the rhythmicity of the gastro-intestinal tract is graded downward from the mouth to the anus; that is the muscle seg-

[1] *Amer. Jour. Physiol*, 1919, **50**, 57.

[2] *Arch. Int. Med.*, 1920, **26**, 410.

ments nearest the cardia always show the greatest tendency to rhythmic contractions, while those from the pyloric region are slower in starting, indicating that the rate of contraction is greatest at the cardia and progressively decreases toward the pylorus. The same rhythmicity is present as a gradient throughout the entire bowel progressively decreasing toward the lower bowel and according to Alvarez "the underlying gradient of tone might be the essential factor in determining the direction of peristalsis." Alvarez has further demonstrated that there is a gradient of oxidation and carbon dioxide production in the wall of the intestine underlying and giving rise to other gradients of tone and rhythmicity, the process progressing at a more rapid rate in the duodenum than in the lower bowel.

According to this theory stagnation is not always due to a failure in peristalsis but the gradient is here altered by an unequal effect of the toxins on the muscles of the two ends of the organ. These gradients may be reversed by any disease, irritation or inflammation or by intoxication affecting the musculature of the lower portion of the gastro-intestinal tract, increasing the activity of this area above that of the upper portion and thus reverse peristalsis, retention and vomiting may be explained.

Meltzer first called attention to the law of *contrary innervation* in its relation to the stomach and intestine. According to this law stimulation of one segment of the intestine causes a contraction above and inhibition of the intestines below the stimulated area. He defines gastric and intestinal colic as being caused by a disturbance of the law of contrary innervation, namely, that the caudal end remains contracted and stationary, while the cephalic end contracts and progresses forward. The area between the two contracted portions becomes gradually smaller while the contents remains unchanged and in consequence there is increased tension leading to severe colicky attacks.

Etiology.—Gastric neuroses may be primary or secondary; they are primary when the seat of the nervous disorder is inherent in the stomach itself, and secondary when the nervous mechanism of the stomach is reflexly affected either from the brain, spinal cord, or some other organ, such as the liver, kidneys, etc. Thus, a severe pain, such as kidney colic, may reflexly affect the stomach, causing vomiting; menstrual disorders, as well as sexual disorders in males, may have a marked reflex effect upon the gastric functions. It was shown by Gould that severe eye-strain may have a marked influence in this regard. It has been suggested by Dock, that focal infections may be the cause of certain functional disorders and that treatment in a case of bulimia by removal of infected teeth and the treatment of nasal and sinus disease resulted in a cure. On the other hand, gastric neuroses may in turn reflexly affect other organs, causing such symptoms as headache, palpitation and insomnia.

Occurrence.—The writer has classified the cases of gastric neuroses occurring in his practice during a period of some years; to obtain a clearer view of these cases, the records of private cases and hospital practice have been used. This was deemed advisable because comparatively few forms of gastric neuroses are seen in hospital wards. Of 2000 patients suffering with various forms of gastric disease, 1592 (79.6 per cent.) represented one or more forms of nervous disorder, while 408 (20.4 per cent.) had organic

disease. In a smaller series of cases more recently analyzed, it was observed that gastric neuroses are much less frequent now, than was formerly supposed, and that but 45 per cent. of the cases could be classified as neuroses, while 55 per cent. represented organic diseases. This change in the relation of two conditions, is due to the fact that many cases which were formerly classified as neuroses are known now to be due to definite pathological change.

In order that a gastric neurosis may exist, some predisposition, *i. e.*, a neurotic condition in the individual must exist. This is frequently first manifested by nervous symptoms directed to other organs, the stomach only later becoming involved. In this series of cases the early nervous manifestations were first noted in 38 per cent. in organs other than the stomach, while in 62 per cent. the stomach itself was first involved. The manner of development of these affections is often peculiar, at times beginning suddenly, often without any apparent cause or error in diet, persisting for a longer or shorter period, and then perhaps terminating abruptly, at other times coming on slowly, progressing rapidly and terminating when least expected. Heredity plays an important role in gastric neuroses. Among our observations, 70 per cent. of the patients gave a history of either some functional or some organic hereditary nervous tendency. In 32 per cent. the disorder was directly dependent upon some shock, anxiety, or vice, while in 18 per cent. no known cause could be discovered.

Most of these affections are more frequent in females than in males, more often in men of the higher classes, and about equally in females of the lower and higher classes. In this series of cases 54 per cent. were females and 46 per cent. males. The chief factor in the production of these conditions in males is overwork, worry, and excesses, especially overindulgence in drink, 29 per cent. of the patients giving a distinct alcoholic history. The chief causes in women are disorders of menstruation and reproduction, anxiety, sorrow, and disappointments. The predominance in this sex is due to the mode of living and peculiar affections.

Age.—The neuroses rarely begin in old age. They occur most frequently between the twentieth and fortieth year. The following table shows the age in the gastric neuroses in this series:

Year.	Cases.	Per cent.
1 to 20	232	14.5
20 to 30	354	22.5
30 to 40	404	25.0
40 to 50	339	21.5
50 to 70	175	11.0
60 to 70	88	5.5

The neuroses occur as frequently in the robust and well-nourished as in the broken-down and enfeebled individual. After persisting for some time neuroses interfere with the general health, frequently occasioning emaciation; this condition, however, is secondary in most instances and is not a predisposing factor in the etiology. The symptoms of a general neurosis are usually present, *i. e.*, irritability, lassitude, insomnia, depression, and a feeling of malaise. Hyperesthesia or anesthesia often

exists in certain parts of the body. The subjective symptoms are changeable and capricious, exhibiting protean changes in rapid succession. The digestion is usually, as Boas states, in a condition of "labile gastrointestinal function." The digestive complaint is frequently independent of the quality and quantity of food ingested, and without any connection with its digestion; errors of diet are not necessarily followed by aggravation of the symptoms. Periodic attacks of discomfort often alternate with unaccountable periods of well-being. Frequently sudden changes take place in the secretory or motor functions of the stomach, or in both, so that a superacidity may quickly give way to a subacidity and a motor insufficiency to a hypermotility. The pain which may be present is diffuse and often bears no relation to the digestion of food.

Gastric neuroses are usually polysymptomatic, more rarely monosymptomatic in character. In the first form there is a multiplicity of symptoms, while in the latter but one symptom is observed. Neuroses rarely present the same form during their entire period, and a monosymptomatic neurosis is not infrequently converted into the polysymptomatic form. A characteristic feature of gastric neuroses is the fact that the symptoms vary so frequently, which is often of great assistance in differentiating between this class and organic disease.

Classification of Gastric Neuroses.—The classification into secretory, sensory, and motor neuroses, so often used, has not been found satisfactory and the following modification is suggested:

Monosymptomatic Gastric Neuroses

Irritative or Vagotonic Group.	*Depressive or Sympatheticotonic Group.*
Superacidity or hyperchlorhydria.	Subacidity or hypochlorhydria.
Supersecretion or gastrosuccorrhœa.	Anacidity or achylia gastrica.
Gastromyxorrhœa.	Akoria.
Bulimia.	Anorexia.
Parorexia.	Sitophobia.
Gastralgokenosis.	Incontinence of pylorus.
Gastralgia.	Atony.
Hyperesthesia.	
Rumination (merycism).	
Regurgitation.	
Eructatio nervosa.	
Vomitus nervosus.	
Nausea nervosa.	
Cardiospasm.	
Pylorospasm.	
Pneumatosis.	
Peristaltic unrest.	

Polysymptomatic Gastric Neuroses

Nervous dyspepsia.

Diagnosis.—This may be very difficult, as frequently these conditions envelop some organic disease, the nervous symptoms being so much more prominent that the actual disease becomes entirely masked. In order to establish the nervous character of a gastric disorder, all organic diseases must be excluded, and this is frequently a most difficult task. In the monosymptomatic forms the diagnosis is usually simple, especially if the examination of the gastric contents and functions shows a normal condition. The patient frequently has a hereditary nervous tendency or

a weakened nervous system or neurotic habit. The disease is frequently either characterized by peculiar periodical or paroxysmal attacks, with many unaccountable periods of well-being, or by an absence of subjective symptoms even upon the ingestion of indigestible food.

The diagnosis of the polysymptomatic forms is more difficult. In these the symptoms that are frequently found in severe organic diseases may be interwoven and combined with the gastric neuroses; a further difficulty arises from the fact that organic disorders are often accompanied by nervous symptoms, and a most careful investigation may be necessary. Nervous dyspepsia is the most typical example of the polysymptomatic neuroses with a multiplicity of symptoms seldom found in its frequency in organic diseases of the stomach. The nervous dyspeptic himself often indicates the diagnosis of this condition, and one need only listen to his story attentively. Objective signs may be absent, or, when present, may mislead one; thus a slight dislocation of the kidney or a slight gastric atony would be insufficient to account for the symptoms present. In the diagnosis of these conditions the appearance of the attacks without apparent cause and the intervals of well-being are most striking. The fact that as a rule the complaints of the patient bear no relationship to the quantity and quality of food ingested, but are mainly dependent upon overexertion, mental disturbances, and excitement is of greater value in the diagnosis. The conditions are often relieved or improved by change of scene or relaxation.

When it is impossible to gain a clear idea of the condition, Boas advises the functional testing of the stomach. The patient is given a very digestible diet, such as is usually prescribed during the third week of an ulcer treatment. The subjective symptoms are noted while the patient is on the diet, during a period of from three to four days; then additions are made gradually, such as sauces, vegetables, dessert, and raw fruits. An exact record is again made, and by comparing the symptoms during the first and second period the presence of an organic or nervous gastric disorder will be indicated. In the latter condition the symptoms not only often diminish, but frequently disappear entirely during the second period, while in the former they are apt to increase. Boas also advises the frequent testing of the motor and secretory functions of the stomach, which when found to be constantly normal are often alone sufficient evidence to indicate the neurotic nature of the disorder.

Prognosis.—The prognosis in neuroses of the stomach is very favorable, provided the condition is treated early and the cause discovered and removed. Relapses, however, are frequent if care is not taken to regulate the daily regimen and maintain, so far as possible, a stable condition of the general nervous system. It is not uncommon, when relapses do occur, that some nervous manifestation is produced other than that which was originally present. In the series of 1592 cases there were 752 (47 per cent.) that gave a history of one or more relapses; of these, 321 (20 per cent.) had one and 431 (27 per cent.) more than one relapse; in the remaining 840 no evidence of any former attacks could be obtained.

Treatment.—In this it is necessary to remember that one is dealing with patients whose imagination is easily influenced in directions other

than normal; for this reason the personal influence of the physician himself will have much to do with the patient's recovery while great benefit may be derived in many instances by psychotherapy. It is always important to make a most careful and complete examination to convince the patient that there is no organic disease. A change of scene is often important, and specific rules as to the mode of living and diet should be insisted on. In some cases sanatorium treatment is most desirable. The diet should be carefully regulated, and especially in badly nourished patients the aim should be to strengthen the individual and increase the body weight. For this purpose the physical methods of treatment are most serviceable and should be used. Of these, massage, cold and warm douches, packs, poultices, electricity, douching and lavage of the stomach play an important role.

Hydropathic treatment is very useful and should be adapted to the constitutional condition rather than to special symptoms. This treatment must be tonic and stimulant and includes cold sponging with rubbing, cold compresses, the half or full cold bath, the Scottish douche, and Winternitz's compress. When sanatorium treatment is impossible or impracticable, a sojourn at the seashore or mountains, with specific directions as to the mode of living, rest, exercise, and diet, often proves serviceable. A cure at some mineral spring is often beneficial, provided the proper spring is selected and specific directions given as to drinking the water and the mode of living to be followed. In no instances should patients suffering with nervous stomach troubles be permitted to tell others of their condition. In severe forms a rest cure, with isolation of the patient, should be resorted to, as most remarkable results can often be achieved by it.

The nervous dyspeptic should be taught to rely more upon proper hygienic measures than upon drugs, as but few drugs have any marked influence in these cases. Of these remedies the bromides, preparations of valerian, arsenic, and codeine are most useful.

HYPERACIDITY OR HYPERCHLORHYDRIA

By the term hyperacidity is meant an excessive flow of gastric juice or, more correctly, an increase in the secretion of the hydrochloric acid produced by the gastric mucous membrane during the process of digestion. It has been questioned whether hyperchlorhydria should be termed a distinct disease, inasmuch as the excess of acid is simply a symptom observed in a number of gastric disorders and due to a variety of causes; yet the symptoms associated with this condition are so definite and so often embrace all subjective manifestations that we are forced to treat this condition as a special clinical entity. Yet it must be noted that although hyperchlorhydria is in many instances a secretory neurosis, in a large number of cases it is associated with some definite lesion. The significance of the term hyperchlorhydria has materially changed during the past few years. Formerly this condition was recognized whenever the hydrochloric acid of the gastric contents after an Ewald test meal exceeded 0.2 per cent. whether symptoms were occasioned or not. It

was realized however, that many patients have a greater acidity than 0.2 per cent. without any symptoms of hyperacidity, and that on the other hand symptoms of hyperacidity may exist in cases of hypochlorhydria. The same amount may indicate hyperacidity in one individual and not in another, showing that individual variations exist in the normal percentage, and that we cannot always draw a sharp line between the normal and the hyperacid state. The condition has been explained in two ways; according to some writers, the stomach of each individual has its own degree of acidity, and thus may perform its function with an acidity which is insufficient or more than sufficient for another. Any increase in this normal proportion of acid will render this particular gastric secretion superacid for this individual and occasion symptoms of hyperchlorhydria. Another explanation is that the symptoms of hyperchlorhydria are due in these cases to a hypersensitiveness or hyperesthesia of the gastric mucosa to hydrochloric acid. Stockton pointed out that the gastric mucosa is not only often intolerant to an excess of hydrochloric acid, but often to a normal or subnormal percentage of acid. Steele confirmed the observation and went a step farther to show that the hyperacid condition of the gastric contents is not alone capable of producing the symptoms in hydrochlorhydria; according to him there must be some other condition present occasioning the gastric hyperesthesia, such as ulcer, retention, hypersecretion or a sensory neurosis.

Rehfuss has shown that normal individuals respond differently to their test meals. Some respond with an excessive hypersecretion, the so-called hypersecretory type; some are sluggish, the hyposecretory type, while a certain number approach the normal isosecretory type. High acid figures are obtained in health and according to Rehfuss in a large group of normal individuals with hypersecretion.

In health there are alternate cycles of activity and rest; digestive and interdigestive periods. In the *digestive* period psychic stimuli produce a psychic secretion which is later augmented by a true chemical secretion. At the beginning of peristalsis there is a gradual increase in acidity until this reaches a certain height, then active tryptic regurgitation takes place, neutralizing this acidity to a more or less degree.

The *interdigestive* period is observed typically in the empty stomach; the total acidity falls and the percentage of free HCl is quite low. At this period bile and pancreatic secretion are usually present in the gastric contents.

Rehfuss emphasizes the fact that the highest curves of acidity are present in health and that a very high acidity is frequently obtained in individuals without being accompanied by any gastric discomfort. In certain diseases, such as ulcer of the stomach, which are frequently accompanied by hyperacidity, the symptoms, according to Rehfuss, are by no means accounted for by the hyperacid state, but are produced by a vagatonia and are induced by a persistent disturbance in the harmonious sequence of the digestive and interdigestive phases. Crohn and Reiss have shown that clinical improvement may take place in cases of hyperacidity (especially in ulcer cases) no matter whether the hyperacidity is reduced or not. The same may be said in regard to cases of hypersecretion.

The relief in some instances must be due to the disappearance of the accompanying pylorospasm, but this does not account for the relief in those instances in which the gastric motility remains normal. The explanation must be found in the quieting effect upon gastric contractions reducing the tonus of the stomach, which need not, however, necessarily be accompanied by a reduction in acidity or secretion. The experiments tend to indicate that the symptoms ordinarily attributed to the excess of acid are not necessarily due to this factor, but must be attributed in many instances to other conditions.

Rogers, Rohe and Ablahadran have demonstrated that the endocrine system plays an exceedingly important role in the stimulation and inhibition of the gastric secretion. According to them a saline or alcoholic extract of the thyroid gland contains some non-coagulable material, which is a vigorous stimulant to the hydrochloric acid of the gastric secretion and produces its effect by intensification of the functions of the terminal filaments of the vagus, while extracts from the adrenal gland inhibit the hydrochloric acid of the gastric secretion. this being produced by intensification of the inhibitory function of the sympathetic. That the nervous system plays a most important role in the production of hyperchlorhydria there can be no doubt, as it is through the involuntary nervous system that the effect of the internal secretions upon the gastric secretion is regulated.

By injecting the extract of the thyroid or parathyroid glands or pyloric mucosa, Rogers produced a marked increase in flow of the gastric secretion which could be inhibited by an injection of atropine or an extract of the adrenal gland. After prolonged stimulation the sympathetic proper becomes fatigued, allowing the vagus full play free of all inhibition, in consequence of which hyperacidity, hypermotility, and pylorospasm are produced and if this is much prolonged even ulceration may ensue.

Etiology.—Hyperchlorhydria is the most frequent of all gastric disturbances. It is frequently observed in young and middle-aged persons, while it is rarer in older individuals. It is found to a slight degree more frequently in females than males and among the better and wealthier classes than among the poor. This is due to the fact that mental strain and worry are often direct factors in the production of this disorder. Jaworski points out its frequency among the Polish Jews; we have observed it as a most frequent condition among the Hebrews of this vicinity. The following etiological factors may be noted:

1. Primary disturbance of the gastro-intestinal tract.
2. Constitutional and organic disease beyond the gastro-intestinal tract itself, including focal infection and reflex causes.
3. Nervous affections.
4. Disturbance of the endocrine glands.

In the first group are those forms due to primary disturbance of the gastro-intestinal tract, among which are ulcer of the stomach, pyloric obstruction due to benign stenosis, acid gastritis, gastro-intestinal atony and chronic constipation; hyperacidity due to indiscretions in diet, food, drink and tobacco is included in this group. In the series of 542 cases of hyperchlorhydria, studied by us, 114 cases belong to this group.

The second group included those cases due to constitutional and organic disease beyond the stomach itself, but including focal infections and reflex causes. Among these are cholelithiasis, nephrolithiasis, chronic appendicitis, anemia, cerebrospinal diseases, abdominal adhesions and various genito-urinary affections; 239 cases are represented in this group.

The third group includes the cases of nervous origin. These are due to mental strain, overwork, prolonged worry and mental fatigue and are observed in neurasthenia, hysteria, and mental affections. There are 161 cases in this group.

The fourth includes the hyperchlorhydrias due to disturbances of the endocrine glands as disturbances of the thyroid and parathyroids. There are 28 cases represented in this group.

As hyperchlorhydria may be caused by many conditions, great care must be exercised to determine the nature of the primary affection. This is not always a simple task for the primary disease may be exceedingly obscure and latent. We frequently observe hyperchlorhydria due to appendicitis or cholelithiasis relieved entirely by surgical intervention, after medical treatment has failed.

After the primary affection has been discovered and appropriate treatment directed toward the cause, much can be done by instituting the proper dietetic régime. It must be remembered that the restricted diet does not in many instances diminish greatly the hyperchlorhydria, but in lessening the irritability of the gastric mucous membrane, by reducing the contractions and by lessening the tonus of the stomach, gastric discomfort is relieved.

The observations of Crohn and Reiss point definitely to the fact that only in a fair proportion of cases is a reduction in the acid in hyperacidity and in hypersecretion possible and that clinical improvement may take place no matter whether the hyperacidity is reduced or not.

The following table represents the cases of hyperchlorhydria, tabulated according to age and sex, presenting the various etiological factors.

Hyperchlorhydria due to	No.	Males.	Females.	Ages in years. 10–30.	30–60	50–70.
1. Primary disturbance of the gastro-intestinal tract .	114	65	49	48	45	21
2. Constitutional and organic diseases beyond the gastro-intestinal tract . .	239	138	101	81	95	63
3. Nervous affections . . .	161	63	98	52	66	43
4. Disturbance of the endocrine glands	28	16	12	13	10	5

Pathology.—As hyperchlorhydria is largely a sensory neurosis, no anatomical lesion is present in the greater proportion of cases. According to Hemmeter, who examined fragments of mucosa found in the wash water, there is in more than one-half the cases of hyperacidity "a proliferation of the glandular elements and increase of oxyntic or border cells."

Symptoms.—The *subjective* symptoms usually appear gradually; they consist of acid eructations, heartburn, and pain and burning in the stomach. Acid eructations usually appear at the height of the paroxysms

of gastralgia, and their appearance is accompanied by a passing relief from pain. If portions of the acid secretion of the stomach are eructated, the mucous membrane of the œsophagus is subjected to this irritation, and heartburn develops. This symptom usually appears after eating acid foods, and is frequently relieved by taking milk, meats, and eggs. The pain may vary from a severe pressure in the stomach to a very acute pain, and may extend into the back between the shoulder-blades and pass under the sternum to the pharynx (pyrosis hydrochlorica). It is not continuous, but appears at certain periods with intervals of complete relief, usually from two to four hours after meals, depending upon the quality and quantity of food taken. In a very small number of cases the pain supervenes immediately upon eating, as occurred in 9 of the series (1.6 per cent.). The symptoms continue for a variable period of time, disappearing in the course of an hour or persisting for many hours. Pain is much more easily induced by starchy foods than by protein foods, more quickly by light meals than by heavy ones, and is usually relieved by the ingestion of food or by neutralizing the acid by means of some alkali. Paroxysms of pain (gastralgia) occur in a certain proportion of cases; they develop gradually, beginning as a feeling of pressure and becoming more severe. As a rule, the pain disappears at night upon lying down, and does not begin again until several hours after breakfast.

The severe gastralgic paroxysms are not commonly found after every meal. They are accompanied not only by intense pains in the epigastrium, but also in the back; they are partially relieved by the acid eructations and entirely by the vomiting of the acid secretion, which burns the throat and numbs the teeth as it passes over them. In some cases the seizures may be very mild, and in other cases they recur irregularly at intervals of days. In this series of 542 cases, gastralgic seizures occurred in 176, *i. e.*, 32 per cent. A sensation of burning in the stomach is frequently observed; this is felt in the epigastrium, and may extend to the back. It is relieved by the same measures as those which relieve the pain, namely, by alkalis or the taking of some form of food. In this series there were 221 that complained of this sensation, *i. e.*, 40 per cent. The appetite is usually good, and as eating usually relieves the symptoms, the patient often accustoms himself to eat frequently; small quantities will, however, often satisfy the patient. In 124 (21 per cent.) of the cases the appetite was increased, in 357 (66 per cent.) it was normal, and in 61 (13 per cent.) it was diminished. The thirst is not greatly increased, although the reverse is stated by most authorities. In this series thirst was only increased in 31, *i. e.*, 6 per cent.

The bowels are frequently constipated, as occurred in 164 of the series, or 30 per cent. Occasionally constipation alternates with diarrhœa, as occurred in 7 of the cases (1.3 per cent.).

The *objective* findings may be divided into two classes, those presented by the physical examination and those obtained by the examination of the vomited material and gastric contents. The patient, as a rule, is in good general health, has lost but little flesh, and the general nutrition is not usually disturbed; the abdomen is not usually sensitive to pressure, and painful areas are not apparent except perhaps during

the attacks of pain, when the stomach may be found distended and sensitive to pressure. Vomiting is not frequent; it usually occurs when the paroxysms of gastralgia are present, and then at the height of the attack; relief is obtained by vomiting, and the pain disappears. This symptom occurred in 86 of the cases, or 15 per cent. The vomited matter is very acid, which is detected even by the patient himself; on examination this material is found to contain large quantities of free hydrochloric acid. The examination of the gastric contents after a test meal usually reveals normal or hypermotility. Six hours after a Riegel test dinner the stomach is usually empty; one hour after a test breakfast it contains only a small quantity of gastric juice. In 30 per cent. of this series there was an atony of the stomach in which more or less retention was observed. The gastric juice shows a very high degree of acidity; the starch digestion is imperfect, and rather large quantities of amidulin are found. On the other hand, the protein digestion in the stomach is complete and peptonization is more rapid than under normal conditions, so that none or but few undigested meat fibres are found in the gastric contents.

Schüler has pointed out that the specific gravity of the gastric juice is diminished in hyperchlorhydria. According to this observer it is usually below 1.016, the normal specific gravity varying between 1.016 to 1.020. The observations in 14 cases as to the specific gravity of the gastric contents in this condition range between 1.008 and 1.014, although higher figures are found, as in 3 of this series between 1.019 and 1.022.

Absorption in the stomach is said to be more rapid in hyperchlorhydria than under normal conditions.

The *urine* is at times alkaline and contains a precipitate of phosphate, especially after severe attacks of vomiting. The acidity of the urine is diminished proportionately to the increase in acidity of the gastric juice, and the chlorides are also diminished in quantity.

Diagnosis.—This is established by careful investigation into the subjective symptoms together with the results obtained from analysis of the gastric contents. These symptoms consist of acid eructations, heartburn, burning and pains in the stomach, the pain appearing from two to four hours after meals, relief being obtained by the ingestion of food and by neutralizing the acid with alkalis. The examination of the stomach contents after a test meal reveals an increase in free hydrochloric acid. This is best determined by a fractional analysis, for the hyperacid secretion may appear after an hour and occasionally earlier, so that its appearance would be overlooked should we rely entirely upon the hour extraction. On fasting, the stomach is found nearly or almost completely empty. Hyperchlorhydria must be differentiated from chronic hypersecretion, ulcer, acid gastritis, atony, and cholelithiasis.

Chronic hypersecretion is distinguished by the intense gastric pains appearing frequently at night, the more frequent vomiting, and the appearance of large quantities of gastric juice (100 cc. and more) in the fasting stomach. *Ulcer* of the stomach (without hemorrhage) is differentiated by the presence of the circumscribed epigastric and dorsal areas of pain. The pain in ulcer is proportionate to the quality and

quantity of the food taken, which is not usual in hyperchlorhydria. Occult blood is frequently found in the feces in ulcer, but not in hyperchlorhydria. *Duodenal ulcer* is distinguished by the characteristic remissions in pain, extending over longer or shorter periods; by the painful area which is absent in hyperacidity, and by the presence of occult blood in the stools. The differential diagnosis between these two conditions is very difficult at times, as hyperacidity usually accompanies ulcer of the stomach and duodenum; the greater irregularity of the symptoms in hyperchlorhydria and presence at least of some of the definite symptoms of ulcer will usually lead to a correct diagnosis. In doubtful cases, Boas advises that the patient undergo the rest treatment for ulcer; a favorable outcome rather indicates the presence of ulcer.

Hyperchlorhydria is distinguished from an *acid gastritis* by the constant absence of mucus in the gastric contents, and from *atony* by the absence of symptoms of retention. In *cholelithiasis* the pains are not relieved by the ingestion of food or the administration of alkalis, and radiate to the right toward the hypochondriac region and are in no way dependent upon the time of the ingestion of food, whereas the pains of hyperchlorhydria usually appear at the height of digestion, *i. e.*, from two to four hours after meals.

Prognosis.—This is usually quite favorable as to the relief of the symptoms, especially if the condition is of recent origin; in protracted cases the prognosis is less favorable. Attention has been called to the observations of Crohn and Reiss and our findings are entirely in accord with these, that clinical improvement may take place in cases of hyperacidity whether the hyperacidity be reduced or not, indicating that the symptoms ordinarily attributed to the excess of acid are not necessarily due to this factor but must be attributed in many instances to other conditions. As hyperchlorhydria may be symptomatic of many affections the prognosis must depend largely upon the nature of the primary condition. On the other hand, relapses are frequent even though there is apparent cure; for an excess of acid secretion may exist even though the patient is free of all symptoms of hyperacidity.

Treatment.—In this the diet plays the most important role, it being essential that the food should be given in such a form as not to produce any irritation to the mucous membrane of the stomach. This includes the removal of all causes of irritation, the prohibition of alcohol, all acids, including organic acids, all spices and condiments, such as ginger, pepper, mustard, and horseradish. All foods to which vinegar or lemon-juice have been added should be interdicted; all hard substances which are apt to irritate the stomach, such as nuts, should be avoided; food must be thoroughly masticated and should be taken neither too hot nor too cold. While some authorities recommend a diet consisting almost exclusively of proteins to neutralize as much acid as possible as the proteins possess the power of combining with free hydrochloric acid, others maintain that while the proteins possess this power, they stimulate the flow of acid: some, such as raw beef, beef-juice, and beef extract, more than others, such as well-cooked meat.

On the other hand, various authors have recommended a carbohydrate

diet in preference to a protein one. Some prefer a liberal mixed diet, consisting of proteins, fats, and carbohydrates. The following table taken from Bickel presents the foods which slightly and the foods which strongly excite gastric secretion:

Foods slightly exciting acid secretion.

Liquids: Water, alkaline water, tea, cocoa (rich in fats), milk (rich in fats), cream, and egg-albumen.
Condiments: 0.9 per cent. of salt solution.
Solids: Cooked meats, fats of all kinds, cooked vegetables, such as potatoes, asparagus, cauliflower, spinach, white beets (all in purée), starch, sugar.

Foods strongly exciting acid secretion.

Liquids: All alcoholic and carbonated drinks, coffee, cocoa (poor in fats), skimmed milk, beef-tea, beef extract, strongly seasoned soups, yolk of eggs, hard-boiled eggs, beef solution.
Condiments: Pepper, cinnamon, mustard, cloves, paprika, salt in concentration.
Solids: Raw or slightly cooked beef, dark meats, salted meats (pork, pickled meats, smoked fish), dark breads.

The carbohydrate foods which are allowable are the more digestible vegetables, such as mashed potatoes, spinach, asparagus, peas, and carrots, strained and eaten in the form of purées, also the digestible farinaceous foods, such as rice and grits. Strauss has recommended the administration of a solution of sugar; this food can be best given in most instances in the form of some baked cake in which part of the starch has become dextrinized by baking or roasting. Strauss and Aldor have advised the use of fats, inasmuch as they tend to lessen the acidity of the gastric secretion. They are best given in the form of butter, cream, olive oil, and the like. Of the fluids, milk, cocoa, and alkaline mineral waters, such as Apollinaris, Vichy, and Seltzer, are especially useful; the carbon dioxide produces a sedative effect and lessens the secretion of acid. These waters may be used to dilute milk.

In arranging the diet it has been found best in dealing with patients taking but little nourishment to allow them to eat at frequent intervals; if, however, large meals are consumed, it is advisable to permit only three meals a day, allowing the stomach to rest in the intervals. In marked forms of nervous hyperchlorhydria a purely vegetable or milk and vegetable diet has been recommended by certain writers; the vegetables should be eaten in the form of purées. Some attach great importance to a salt-free diet in hyperchlorhydria, believing that a high percentage of muriatic acid may be reduced by a diet free of salt. In advanced cases, with marked emaciation and prominent nervous symptoms, a complete or modified rest cure will accomplish excellent results; in these cases milk and egg-albumen should be the only food given at first, gradually increasing, and finally allowing easily digestible solid food. In severe forms of hyperchlorhydria great relief has been obtained by a Sippy cure, even though there was no indication of ulceration.

The following list, taken from Friedenwald and Ruhräh,[1] gives the foods which are allowable and those which are forbidden in hyperchlorhydria: Allowable: Eggs, soft boiled, hard boiled, or poached. Meats, boiled or broiled; brains, raw scraped beef, boiled or broiled beef, broiled

[1] *Diet in Health and Disease*, sixth edition, p. 908.

steak, roast mutton, broiled chops, roast lamb; boiled, broiled, or roasted chicken; broiled or roasted squab, roast turkey, broiled or roasted birds. Farinaceous food: Rice, cornstarch, sago, tapioca, arrowroot, hominy, grits, vermicelli, cream of wheat, stale wheat bread, toast corn bread, pulled bread, zwieback. Fruits: Baked or stewed apples, stewed apricots, stewed peaches, stewed pears, stewed prunes. Fatty foods: Butter, cream, pure olive oil. Drinks (taken mainly between meals): Milk, buttermilk, malted milk, peptonized milk, milk with lime-water, milk with Vichy, milk flavored with tea, milk flavored with coffee, kefir, koumyss, junket, whey, cocoa, albumin-water, water (not with meals), hot water. Vichy, Apollinaris, Poland, Lithia water, Carlsbad.

They must not take: Soups, fried foods, pork, veal, stews, hashes, corned meat, liver, kidney, duck, goose, sausage, crabs, lobsters, preserved fish, smoked fish, salmon, salt mackerel, sardines, cauliflower, celery, cocoa, radishes, cucumbers, sweet potatoes, beets, tomatoes, acid fruits, salads, hot bread or cakes, nuts, candies, pies, pastry, strong tea, coffee, alcoholic stimulants, ice-water, ice-cream.

Hygienic Measures.—These should never be neglected in the treatment of hyperchlorhydria. Those patients who have been fatigued by overwork should be ordered rest, and those who are worn out by mental strain and excitement are often best ordered away to the country, seashore, or mountains; physical exercises, out-door life, and cold sponge baths are often serviceable adjuvants; warm poultices or Preissnitz compresses are frequently useful in the relief of pain.

Gastric lavage is rarely necessary in the simple cases although it is often of benefit in severe and obstinate forms. It is best practised late in the evening, three or four hours after the last meal, or on an empty stomach in the morning; douching of the stomach with a solution of silver nitrate is often beneficial; 500 cc. of a 1 to 2000 solution is allowed to enter the stomach and washed out thoroughly with normal salt solution.

Medicinal Treatment.—Alkalis are employed to neutralize the excess of acid. Of these, the bicarbonate of soda, calcined magnesia, magnesia carbonate, calcium carbonate, and the phosphate of soda are most frequently utilized. Calcined magnesia has an advantage over bicarbonate of soda, as the former neutralizes four times as much acid as the latter; it has the additional advantage in that it is distinctly laxative and is therefore especially useful when constipation is present; the doses of the alkali should be, so far as possible, proportioned to the heaviness of the meal as well as the degree of hyperacidity. The alkalis should be administered when the discomfort begins to manifest itself, *i. e.*, about two hours after meals. Whenever symptoms of alkalosis appear and when the alkaline antacids are badly borne, the use of the neutral antacids (phosphates of calcium and magnesium) is to be recommended. Either should be administered in from 1 to 2 teaspoonful doses three times daily after meals. Of other drugs found useful are:

1. Atropine, which inhibits gastric secretion. This remedy can be administered in the form of the extract of belladonna or atropine.

2. Nitrate of silver in solution, which tends to diminish the gastric hyperesthesia.

3. Bismuth subnitrate and carbonate, which may be administered in large doses and which exert a beneficial, largely mechanical, effect on the gastric mucosa.

4. Hydrogen peroxide is also useful and may be given in one-teaspoonful doses in a glass of water after meals. Magnesium peroxide has been found beneficial.

5. The nerve sedatives, such as the bromides, valerianates, and sumbul, which relieve the gastric hyperesthesia. In those cases in which symptoms of hyperacidity exist and in which the gastric secretion shows a normal or lessened amount of acid the sedatives are more valuable than the alkalis. Benzyl-benzoate is also helpful in this condition.

6. Nux vomica: While the bitter tonics are to be avoided, as a rule, in hyperchlorhydria, Musser[1] advised the administration of nux vomica in ascending doses in those cases in which the symptoms of hyperacidity are due to a sensory neurosis; he had uniformly good results from this.

7. Olive oil: This may be given in tablespoonful doses before meals or about two hours after meals.

Inasmuch as constipation is sometimes the cause of hyperchlorhydria, a correction of this will often give permanent relief and this is often best accomplished by diet rather than by drugs.

GASTROSUCCORRHŒA OR HYPERSECRETION OF GASTRIC JUICE

This is a condition in which a constant excessive flow of gastric juice is secreted. The stomach pours out this secretion even when free from food, so that large quantities of gastric juice may be found even in the morning before the ingestion of any nourishment. This disease was first described by Reichmann[2] in 1882, and afterward more fully elucidated by Riegel in various communications between 1884 and 1893.

The disease is found in three forms: gastrosuccorrhœa continua periodica, gastrosucchorrhœa continua chronica, and digestive gastrosuccorrhœa. There has been considerable diversity of opinion among various authors whether gastrosuccorrhœa should be placed in the category of organic diseases or among the neuroses. There is no question that in most instances this condition is a result of some marked organic gastric affection, as ulcer with obstruction, dilatation, or atony. On the other hand, in a small number of cases the condition can only be looked upon as neurotic; this is more frequently the case with the form known as gastrosuccorrhœa continua periodica than the continua chronica.

Gastrosuccorrhœa Continua Periodica.—By this is meant that condition in which, in addition to the appearance of the acute attacks with a constant secretion of gastric juice, severe gastric pains and vomiting are present. Rossbach[3] called attention to a condition which is closely related to periodical hypersecretion, but in which the attack takes its onset with violent headaches and which he termed gastroxynsis. Periodical hypersecretion may be present as a simple gastric neurosis or as a reflex

[1] *Tran. Assn. Am. Physicians*, 1905, **20**, 193.
[2] *Berl. klin. Wochenschrift*, 1882, No. 40.
[3] *Deutsch. Archiv f. klin. Med.*, 1885, Band 357.

neurosis, secondary to disease of the brain or spinal cord, *i. e.*, progressive paralysis, tabes dorsalis, or myelitis or to chronic cholecystitis or appendicitis.

Etiology.—The causes are various, among which are excessive mental strain, excitement, anger, overindulgence in food, and the abuse of tobacco. At times this condition is found with the crises of locomotor ataxia. The patient with this condition usually presents other nervous symptoms indicating the nervous origin. The disease occurs usually in young people, and more frequently in males than in females. In a series of 1592 cases, 21 suffered with intermittent hypersecretion (1.5 per cent.).

Symptoms.—The characteristic signs of this condition are not only the paroxysmal appearance of the attacks, which take their onset in the midst of perfect health, but also the special character of the gastric contents and vomitus. The attack has its onset early in the morning, usually with lassitude, malaise, headache, loss of appetite, thirst, and pains in the stomach, which become intense and are accompanied by heartburn and acid belching. The pains become spasmodic and more intense, and finally vomiting sets in. The vomited matter is very acid, at first consisting of food and then of gastric juice. The attacks may thus be entirely recovered from, or after a short period of relief others may set in, extending over a period of from a few hours to several days. The vomiting can be prevented at times by the drinking of large draughts of water or by the administration of large doses of alkalis. The quantity of the vomited matter is usually very large in amount, often from 200 to 500 cc., containing at first food particles and afterward consisting of pure gastric juice, which is tinged yellowish or greenish with bile. The material first vomited is usually very acid, often containing 0.3 per cent. or more free hydrochloric acid, but afterward, when admixed with bile, the acidity is greatly reduced to or below normal. The vomited material may contain slight traces of blood, which has no special significance. During the attack, besides the intense pain there is a total loss of appetite, great thirst, and general feebleness; the pulse becomes weak and the patient presents the appearance of great suffering; he becomes pale and breaks out in a cold perspiration. The urine is greatly diminished in quantity and of a high specific gravity, while the bowels are constipated. The attacks vary greatly both as to intensity and duration, sometimes terminating gradually, sometimes suddenly. Between the attacks the patient is usually in good health, free of all disturbances, although at times moderate gastric disturbances exist, such as discomfort in the stomach, acid eructations and heartburn. Gastric analysis at this time usually reveals a hyperacidity, even though symptoms of hyperchlorhydria are not present. The condition known as *gastroxynsis* differs from periodic hypersecretion only in that the headache is severe and persistent. The other symptoms of gastroxynsis are so similar to those of periodic hypersecretion that these cases should be classed in the same category.

Diagnosis.—This is made by the appearance of the symptom-complex described, as well as by the finding of large quantities of gastric juice in the stomach at a time when no ingesta are present. The differential

diagnosis must be made from periodic vomiting and the vomiting occurring in the gastric crises of locomotor ataxia. *Periodic hypersecretion* is distinguished from periodic vomiting by the irregular appearance of the attacks and by the vomiting of large quantities of pure gastric juice, whereas, in periodic vomiting, the attacks appear at regular intervals and the vomited material consists of mucus and bile. From the vomiting occurring in the gastric crises periodic hypersecretion is also differentiated by the appearance of large quantities of acid gastric secretion in the vomit and by the fact that the attacks persist during the night, neither of which is usual in the crises of locomotor ataxia.

Prognosis.—The duration varies greatly; some attacks are short, lasting but a few hours, others extend over a period of days. Sometimes the patient becomes greatly weakened and prostrated; in other instances his general health is not impaired. If the primary cause can be determined and relieved the prognosis is favorable; this is impossible in many instances, and the attacks reappear at varying intervals.

Treatment.—This is, so far as possible, to seek out and relieve the cause. If due to overanxiety or mental strain, the patient should be ordered to the mountains or seashore. Physical exercises should be insisted on, and overindulgence in food and drink and in the use of tobacco prohibited. Hydrotherapy exerts a favorable influence.

In a number of our cases relief was afforded by means of intragastric electricity. In those instances in which the attacks have their origin from a hyperchlorhydria this condition must be treated. For the attack itself the mode of treatment advised by Einhorn is often found serviceable; that is, to administer a moderate dose of bromide just as the attack begins; this method will at times abort an attack. As soon as the attack sets in the stomach should be thoroughly washed out with an alkaline solution, and this may be repeated a number of times during the attack. For the severe pain one is often forced to administer morphine hypodermically, this being the only remedy to be relied upon at times to produce even temporary relief. During the attack the patient should be allowed but small quantities of fluids, water, milk, and egg-albumen; bits of ice may be administered to relieve the thirst; also enemata of normal salt solution may be given.

Gatrosuccorrhœa Continua Chronica.—This is also known as Reichmann's disease, or chronic hypersecretion, and also as chronic continuous secretion of gastric juice. It is characterized by a chronic continuous secretion of gastric juice, even in the absence of food in the stomach, that is in the fasting stomach. This condition may be primary or secondary. It is primary when it occurs as a gastric neurosis independent of any known anatomical change in the stomach; it is secondary when it occurs as the result of some other gastric disturbance, such as ulcer, dilatation, or atony. As continuous hypersecretion is most frequently associated with dilatation, and as the symptoms of both conditions are very similar, many authors deny the existence of this condition as a separate entity and believe that it is simply a form of dilatation. It cannot be denied that most cases are secondary to dilatation.

The difficulty in differentiating between continuous hypersecretion

and dilatation is more evident when we observe that of the six cases of this disease originally reported by Reichmann,[1] but one can be counted a case of chronic hypersecretion, the remainder presenting symptoms of hypersecretion secondary to pyloric stenosis. Riegel believes that continuous hypersecretion is in some instances a perversion of function and really of a neurotic type, in which no organic lesion can be detected. M. Pickardt[2] has reported three cases in which this condition was primary and existed as a pure neurosis, and in which careful investigation failed to present any organic disease of the stomach or motor insufficiency.

Etiology.—The causes are much like those of intermittent gastrosuccorrhœa, namely, great mental anxiety and excitement, indiscretion in the use of food, and the abuse of drink extending over long periods of time. Secondary continuous hypersecretion may arise as a result of dilatation, atony, or ulcer. Primary continuous hypersecretion is a rare disease; it does not occur as frequently as intermittent hypersecretion. In this series of 1592 cases there were 10 cases of primary continuous hypersecretion (0.63 per cent.), 7 in males and 3 in females; 4 were between twenty and thirty years of age, 3 between thirty and forty, and 3 between forty and fifty.

Pathology.—The anatomical changes in these conditions are not always uniform. In some cases no anatomical changes are found. In others a special form of gastritis exists, associated with degeneration and destruction of the peptic cells, while the parietal cells remain normal. Interstitial changes have been observed.

Symptoms.—The subjective symptoms of chronic hypersecretion are pain, burning in the epigastrium, heartburn, acid eructations, nausea, vomiting of large quantities of gastric juice, and increased thirst. These make their appearance gradually, and many patients complain of mild dyspeptic symptoms for years before the true nature of the disease is revealed. At first there is but a slight degree of burning in the epigastrium and heartburn, which gradually intensifies, then pain appears, coming on several hours after meals which is relieved by the ingestion of food. The pain also appears in attacks during the night, a rather characteristic symptom. After the pain has existed for some time, vomiting sets in, the vomitus consisting of a large quantity of a very acid gastric juice.

These symptoms may be mild in some patients and very severe in others; they are apt to appear for a certain length of time and disappear, to recur after weeks or months; in severe attacks the symptoms are present almost daily, and vomiting may occur four or five times a day. The patient loses flesh, the tongue and skin become dry, the appetite is increased in some cases, diminished in others. The attacks of pain can be often lessened by the ingestion of protein food, such as boiled eggs or milk. Constipation is usually present, and the quantity of urine is diminished, the chlorides decreased, and the phosphates increased. The objective signs consist in demonstrating hyperacidity as well as the presence of large amounts of gastric juice in the fasting stomach.

[1] *Berliner klin. Wochenschrift*, 1882, No. 40; 1884, Nr. 48; 1887, Nr. 12.
[2] *Ibid.*, October 30, 1905.

The acidity of the gastric juice after a test breakfast may amount to 80, 90, 100, or more, and the free hydrochloric acid to 0.25 to 0.3 per cent. The protein digestion is good, showing a perfect peptone reaction, while the starch digestion is imperfect, the continuous flow of acid impeding amylolysis. The most important and characteristic symptom is the finding of gastric secretion in a fasting stomach; under normal conditions small quantities of gastric juice may be found in the stomach, but when quantities of 100 cc. or more are present the condition of hypersecretion must be considered, and especially so if it is discovered at a number of examinations. Even with smaller quantities than 100 cc. providing the other symptoms are present, such cases must be classified under the head of chronic continuous gastrosuccorrhœa.

In order to arrive at a more certain diagnosis, lavage should be given the evening before; the next morning the stomach is tested, fasting, so that no portions of former meals may be retained. The gastric secretion obtained from the fasting stomach is usually watery and often contains a small trace of bile; it is of a high total acidity and contains an excess of free hydrochloric acid, the peptone reaction being good, the dextrin reaction absent. In the secondary form of gastrosuccorrhœa continua chronica, dilatation or atony of the stomach is usually present.

Sequelæ.—Of the sequelæ or complications, atony and dilatation of the stomach, with or without ulcer, are the most common. Atony and dilatation often appear after the gastrosuccorrhœa has existed for a considerable period of time; it is only in the earlier stages that the primary nature of the chronic hypersecretion can be determined; when the patient is seen late in the course of the disease, when both conditions are marked, it is often impossible to determine which is primary.

Diagnosis.—This is suggested by the symptoms, *i. e.*, excessive pain occurring several hours after meals and also during the night, with vomiting of large quantities of gastric juice. In addition there is burning in the epigastrium, heartburn, acid eructations, and increased thirst. The diagnosis is made certain by examining the stomach in the fasting state, when large quantities of gastric juice, usually over 100 cc., are obtained, showing an entire absence of amylolysis. It is important to practise lavage on the evening before the morning that the fasting stomach is tested. It is often important to exclude atony and dilatation, which, however, are often associated with gastrosuccorrhœa. In atony a motor insufficiency is observed, while in dilatation the motor insufficiency is so great that food particles are still present in the fasting stomach. This is not the case in gastrosuccorrhœa unless the condition is accompanied by dilatation. Ulcer will be excluded by the absence of occult blood in the feces and of a circumscribed painful area, and the presence of large quantities of gastric juice in the fasting stomach.

Prognosis.—This depends largely upon whether the condition is primary or secondary. If it is secondary to a dilatation, the prognosis is not as favorable as if it were primary, unless some radical procedure is undertaken, such as a pyloroplasty or gastro-enterostomy. When primary, the prognosis is usually not unfavorable, especially if rational treatment is undertaken. Frequent relapses are common, while certain

severe cases are often very protracted and may continue indefinitely, notwithstanding the most rigid form of treatment.

Treatment.—This consists in relieving the irritation of the gastric mucosa and thus diminishing the flow of gastric secretion. Diet is of primary importance and should consist of small but frequent meals, given at intervals of from three to four hours. The patient should be required to eat slowly and masticate his food thoroughly; all irritating substances such as pepper, mustard, onions, and highly seasoned foods should be interdicted. As motor disturbances are apt to occur in this condition, fluids should be administered sparingly. The diet should be made up mainly of proteins, since these foods are well borne. The carbohydrates are poorly digested, and hence must be given only in small quantities and in the most easily digestible forms. All forms of meat are allowable, roast beef, lamb chops, chicken, and broiled steak, but should be finely minced. Of the carbohydrates the best are oatmeal, zwieback, Nestlé's food; purée of potatoes, spinach, etc., may also be allowed. Fats may be permitted to a greater or less degree in the form of good butter, cream, or olive oil. Milk is excellent, and may be taken either alone or mixed with small quantities of tea, coffee, or cocoa. It may also be given with eggs. The foregoing regulations as to diet apply to chronic hypersecretion without dilatation; when ectasia exists the dietetic rules described under this head must be followed.

Lavage of the stomach is a most efficient means of relieving pain and irritation. This is best practised in the morning before the ingestion of food. Instead of lavage Boas recommends emptying the stomach in the fasting state (expression) by means of the tube; while Reichmann believes in lavage of the stomach with solutions of nitrate of silver 1 or 2 to 1000. Penzoldt advises douching with a solution of boric acid, and Einhorn sprays the stomach with nitrate of silver.

The alkalis play a most important rôle in the treatment of the disease; of these, bicarbonate of soda, calcined magnesia, phosphate and citrate of soda are most commonly employed. These are best administered two or three hours after meals, *i. e.*, at the height of digestion. Other remedies which are useful at times are bismuth subnitrate, given in large doses (half a dram), belladonna, and nitrate of silver in solution.

Digestive Gastrosuccorrhœa.—Straus[1] first pointed out that in certain cases of hyperacidity relatively large quantities of a thin, watery, gastric secretion were obtained one hour after a test breakfast. He called this condition digestive or alimentary hypersecretion. Zweig and Calvo[2] investigated this subject more fully, and discovered that the large amounts of contents obtained after the test breakfast do not depend upon motor disturbances of the stomach, such as atony, but rather upon increased gastric secretion. Elsner[3] and Friedenwald[4] have also called attention to this condition. Boas[5] has investigated this question, and

[1] *Deut. Archiv f. klin Med.*, Bd. **56**, S. 120.
[2] *Archiv f. Verd.*, Bd. **9**, S. 262.
[3] *Berlin. klin. Wchnschr.*, 1904, Nr. 25.
[4] *Am. Jour. Med. Sci.*, 1910, **140**, 318.
[5] *Deut. med. Wchnschr.*, 1907, Nr. 33, S. 135.

considers the name digestive gastrosuccorrhœa more appropriate than alimentary gastrosuccorrhœa, because the increased gastric secretion is dependent upon the act of digestion in contradistinction to continuous hypersecretion. In the latter the secretion extends beyond the digestive act, and more or less gastric juice is found in the fasting stomach. It has been suggested that alimentary hypersecretion is not infrequent as a result of gastric ulcer and, on the other hand, that it may at times be transformed into a simple hyperacidity.

Etiology.—This disease occurs most frequently in males. The 12 cases of Boas all occurred in males. In our 14 cases there were 12 males and 2 females, the ages varying between eighteen and sixty-four years.

Symptoms.—An important symptom is extreme emaciation, a loss of from ten to fifteen pounds being not unusual. This loss of flesh is a most important sign, especially since it appears without the slightest tendency to any disturbance of motility of the stomach. The appetite and quantity of food taken may be normal; occasionally, however, both may be decreased. The great loss in weight must be dependent upon the loss of gastric secretion. Amylolysis is extensively diminished and constipation very marked. The subjective symptoms are of much the same character as those in nervous dyspepsia. Patients complain of various sensations in the stomach, pressure, fulness, eructations, excessive flow of saliva; occasionally of violent pains; very rarely, if ever, of heartburn. Nausea or vomiting occurs exceptionally. Marked splashing is observed in the region of the stomach; tender spots painful to pressure are not present; the abdomen is occasionally distended with gas. A diminution in the chlorides and an increase in indican are frequently observed in the urine. This disease is much like atony, and Boas believes that there can be no question but that it has in many instances been mistaken for atony or nervous dyspepsia. In order to determine the presence of this condition, Boas advises a dry test meal. Inasmuch as bread contains 35.5 per cent. of water, he uses Albert cakes containing but 8.9 per cent. of water. If five Albert cakes are given as a test meal and removed from the stomach at the end of an hour under normal conditions, but a small residue will be obtained. In digestive gastrosuccorrhœa, however, 100 to 200 cc. of fluid will be obtained. On standing it forms into two layers, a lower layer slight in amount precipitated to the bottom, and above it a clear or slightly cloudy fluid three or four times as large in amount. The secretion generally shows a total acidity and percentage of free hydrochloric acid, usually not above and often below normal.

In a large proportion of our cases the total acidity varied from 40 to 56 and free hydrochloric acid 35 to 45, which indicates that while in this condition there may be no excess in the acids of the gastric secretion, the secretion is greatly increased in quantity. In other words, there is a hypersecretion but no hyperacidity. The average specific gravity of the gastric juice is 1.006. The secretion presents a more or less marked biuret and sugar reaction, while albumin is not present; erythrodextrin, amidulin, and also the amylum reactions are usually marked. By means of the dry diet the diagnosis is made positive. If the bottom layer of the secretion is large, there must be a motor disturbance present.

Diagnosis.—The symptoms do not wholly point to the condition; the most marked ones are those of chronic nervous dyspepsia with marked emaciation, succussion in the region of the stomach a considerable period of time after meals and after small meals. The symptoms often point to atony, therefore, in order to make an exact diagnosis, three forms of examinations must be used:

I. Examination of the fasting stomach.

II. Examination of the gastric contents one hour after a dry meal.

III. Examination of the gastric contents one hour after a test breakfast.

Prognosis.—This is not unfavorable. Alimentary gastrosuccorrhœa is a gastric affection of nervous origin, which is apt to extend over a long period of time, presenting great variability of symptoms, and with days and weeks of apparent perfect health giving place suddenly to periods of severe distress. That this disorder is purely a form of gastric neurasthenia is manifested by the fact that when the patient is restored to good health the increased secretion is apt to disappear.

Treatment.—The indications are to increase the body weight, to avoid foods that increase the quantity of gastric secretion, and to counteract the imperfect starchy digestion, all three indications being corrected by the diet. It is also necessary to overcome constipation, and this can be accomplished by the same means, namely, by a protein and fat diet, with a small proportion of carbohydrate. In place of sugar, dextrinized food can be utilized as bread; the crust of wheat bread is to be preferred. Fluids should be given plentifully to avoid the irritation of the gastric juice upon the mucous membrane. Alkaline drinks should be taken plentifully during meals. Soups, alcohol, black coffee, and tea should be avoided. Excellent results are obtained by a rest cure of some weeks. Of medicinal remedies, belladonna or atropine may be utilized and alkalis are beneficial.

GASTROMYXORRHŒA

By gastromyxorrhœa is meant a flow of mucus from the stomach. While various observers as Ewald, Riegel, Martius, have shown that small quantities of mucus were occasionally found in the fasting stomach, but little attention was paid to this condition until Dauber[1] pointed out that under abnormal conditions considerable quantities of mucus were secreted by the stomach and found in the fasting state. He called the disease chronic hypersecretion of mucus or gastrosuccorrhœa mucosa. Kuttner[2] investigated the subject farther, and found that the condition is not infrequent, and is often observed in certain patients if lavage is practised on the fasting stomach.

The appearance of small quantities of mucus in the fasting stomach may be regarded as normal; it is important, therefore, to fix a limit to the quantity to be considered normal, and any amount beyond this must be looked upon as pathological. Kuttner regards the recovery of more than 5 cc. of mucus from the fasting stomach pathological, but considers the condition one of gastromyxorrhœa when more than 25 cc. are

[1] *Archiv f. Verdauungskr.*, Bd. **2**, S. 167.
[2] *Berlin. klin. Wchnschr.*, October 30, 1905.

obtained. The condition can only be considered present if the secretion of mucus is constant or reappears at certain intervals. It is important, however, to consider the method by which the mucus is obtained. The patient should be accustomed to the use of the tube, as otherwise the mixture of saliva with the mucus will be so great as to vitiate the results. The method of moving the tube to and fro to induce the expulsion of mucus and the long continuance of the examination will increase the quantity of mucus. In order to arrive at a definite decision that there is an abnormal secretion, repeated examinations should be made. It is perfectly possible, too, that by swallowing saliva and pharyngeal mucus, secretion in the stomach may be excited; on the other hand, there must be a pathological disposition to secrete mucus in such cases, as the mucous membrane of the stomach would hardly react thus to so slight an irritation.

Intermittent Gastromyxorrhœa.—This occurs rarely. Many cases are probably not recognized, as the discomfort is not lasting and the attention of the physician is not called to the condition. In this the increased secretion of mucus occurs at irregular intervals.

Etiology.—Kuttner was unable to find any evidences of locomotor ataxia in the patients whom he investigated. In 2 the attack took its onset with disturbances in the secretions of the nose. He believes, therefore, that there is connection between the affection of the nose and that of the stomach; the mucus of the stomach, however, is not simply swallowed, but in large part due to secretion.

Symptoms.—The attack may begin with prodromal symptoms, headache, loss of appetite, nausea, etc., but more usually in the midst of perfect health, often early in the morning, soon after awakening. The most striking symptoms of this paroxysmal attack is severe vomiting, which is intractable in the true sense of the word, as it cannot be successfully checked by any remedy. The vomited matter consists of large quantities of tough, slimy liquid, finally of bile and intestinal juices, but contains no food remains. Pain in the region of the stomach is not present, or if so it is of no moment. During the attack the stomach refuses to retain food, drink, or medicine. The patient feels wretched, the abdomen is retracted, the pulse small, the tongue dry, and the quantity of urine much diminished. The attack may extend over a period of one day, or may continue from three to five or even twelve days. The attack usually ceases quite suddenly, and after the cessation of the vomiting the patient can again take food without any annoyance. The patient enjoys good health during the interval of the attacks, and often has no or slight dyspeptic symptoms. The gastric contents after a test breakfast in the interval generally show a normal percentage of hydrochloric acid and only a slight amount of mucus.

Treatment.—A distinction must be made between the attack and the patient's general condition. In the beginning of the attack thorough lavage may terminate the symptoms at once, although when they are at their height lavage is valueless, and but little is to be gained by the internal administration of medicine. A hypodermic injection of morphine with atropine is sometimes useful. A condition of collapse accompanying

a severe attack may be so serious, especially in patients with a weak heart, as to demand stimulation. Treatment of the underlying condition is mainly directed to the removal of the neurotic tendency. At times a change of climate and atmosphere, hydrotherapy, massage, electricity, iron, and arsenic may produce a favorable influence upon the disease. Search should be made for a possible cause, either in the stomach itself or in other organs, such as the nose, and treatment should be directed to these conditions.

Continuous Gastromyxorrhœa.—The chronic or continuous form is more frequent than the intermittent.

Etiology.—This condition may be associated with hypersecretion of acid or with various organic diseases, or may exist as an independent functional neurosis. Kuttner has found it associated most frequently with chronic catarrh, as well as with those nervous affections of the gastric mucosa in which there is a marked diminution or entire absence of hydrochloric acid. He also observed it in typical cases of gastric ulcer with or without pyloric obstruction. The seat of origin of the mucus is not known, but it is probably a mixture of the secretion of the superficial epithelium and of the mucous glands, coming in largest measure from the glands of the pylorus.

It is impossible to determine whether this condition is always accompanied by a definite lesion of the mucous membrane, but as it is frequently associated with hypersecretion of acid, it may depend purely upon nervous influences. Twelve cases of this disease have come under the writer's observation, 9 in females, and only 3 in males.

Symptoms.—There are no characteristic symptoms, and the condition may be discovered in some cases in which there are no subjective symptoms. The diagnosis is established by the discovery of large quantities of mucus in the fasting stomach, shown to be the product of the gastric mucous membrane and not to come from other sources, such as the nose, mouth, or pharynx.

Treatment.—Lavage should be practised for the removal of the mucus, provided there is no contra-indication to the procedure; instead of this method of treatment, mineral waters may be utilized, being chosen with reference to the nature of the associated disease, the general condition of the patient, and the various gastric functions.

In contradistinction to gastromyxorrhœa, Kaufmann[1] described a frequent finding in the gastric contents, that is a complete lack of mucus, which he termed *amyxorrhœa gastrica*. This may be due to different causes. Kaufmann calls attention to the fact that the mucus is a protective agent of the gastric mucosa, and that in some of the cases presenting symptoms of hyperacidity, and in which the stomach contents shows no excess of acid, but normal or even subnormal figures of acidity, the lack of sufficient mucus is the principal cause, rendering the mucosa hypersensitive even to secretions of a normal or moderate degree of acidity. The symptoms of hyperacidity disappear under treatment with nitrate of silver, which increases the amount of mucus.

[1] *Am. Jour. Med. Sci.*, 1908, **135**, 207.

BULIMIA

Bulimia is that condition characterized by an abnormal increase in the sensation of hunger. It has also been termed hyperorexia, cynorexia, and lycorexia. Rosenthal believes this disorder is due to an excitation of the hunger centre, and this is probably true in cases of the affection following brain diseases. Stiller considers it due to irritation of the peripheral nerve endings in the stomach itself. It is probable that there are some forms due to lesions of the brain, while others are due to excitation of the nerves in the stomach itself. According to Carlson the sensation of hunger is produced by tonic contractions of the empty stomach.

Etiology.—Bulimia may exist as a primary neurosis or may be secondary to diseases of the stomach or other organs. As a primary neurosis, it is found in neurasthenia and hysteria. It occurs in cerebral tumors, Graves' disease, pulmonary tuberculosis, diabetes, syphilis, intestinal worms, in ulcer and dilatation of the stomach, and in many other conditions. Bulimia is most frequently observed in females between the fifteenth and fortieth years. In the series of 1592 cases of gastric neuroses bulimia occurred in 24 cases (1.5 per cent).

Symptoms.—This condition usually occurs in attacks at irregular intervals, although at times they may appear periodically and extend over a long period of time or may be of short duration and be followed by an attack of anorexia. The disorder comes on as a violent sensation of hunger occurring after meals, in consequence of which the patient becomes exhausted, feels faint, has gastric pains, ringing in the ears, and suffers with vertigo and cold extremities. This continues until some food is taken. A very small quantity of food will ordinarily suffice to overcome the sensation for a period of time; occasionally very large quantities must be ingested to relieve the condition. In 1 case of this series a quantity of food representing 6250 calories was consumed daily. In consequence of the inordinate amount of food, other disturbances of digestion are apt to follow, such as atony, gastritis, and disturbances of the intestines. The gastric contents were examined in 21 of 24 cases; normal acidity was found in 15 (72 per cent.), hyperacidity in 3 (14 per cent.), and subacidity in 3 (14 per cent.); hypermotility was present in 6, normal motility in 12, and atony in 3 cases.

Diagnosis.—Bulimia must be differentiated from acoria and polyphagia. In bulimia there is an abnormal desire for food, but the desire can be satisfied, while in acoria there is an absence of the sensation of satiation. In polyphagia or gluttony, while the appetite remains good, the feeling of satisfaction is delayed to such an extent as to create a constant desire for more food.

Prognosis.—This depends upon the cause, whether it is primary or secondary to some other disorder. The primary form due to neurasthenia or hysteria may be protracted or may disappear suddenly; when secondary, the prognosis depends upon the nature of the primary disease.

Treatment.—In treatment special attention should be directed toward the primary disorder. In those forms due to neurasthenia and hysteria

the nervous system in general should receive special attention. In many cases rest, change of scene, hydrotherapy, electricity, massage, and psychotherapy are effectual means of combating this condition. The diet should be carefully regulated. Patients should be required to eat slowly and masticate the food thoroughly. Nourishment should be taken at frequent and regular intervals, such as every two hours. The food should consist largely of milk, eggs, cereals, boiled fish, the lighter meats, and green vegetables. Fried foods and sweets should be avoided. The bromides have been used advantageously, the bromide of strontium in 15 grain (1 gm.) doses taken three or four times a day, being most useful. Arsenic, codeine, and opium have also been recommended.

PAROREXIA

Parorexia is that condition characterized by a perversion of the appetite. According to the character of the perversion we have: (1) Pica, desire for articles which are not foods, such as chalk and earth. (2) Malacia, desire for spiced food, vinegar, mustard. (3) Allotriophagia, desire for disgusting substances, such as urine and fecal matter.

Pica and malacia are often observed in the same individual. Parorexia is found in neurasthenia and hysteria, occasionally in disturbances of the digestive tract, helminthiasis and gastralgia, and often in the insane. Malacia is frequently observed in chlorotic girls and pregnant women, while allotriophagia is found in the insane. In this series of 1592 cases there were 8 cases of parorexia (0.5 per cent.), 6 being in males and 2 in females; 3 were from ten to twenty, 2 from twenty to thirty, 2 from thirty to forty, and 1 from forty to fifty years of age.

GASTRALGOKENOSIS (PAINFUL GASTRIC EMPTINESS)

Boas has introduced this term to indicate that neurosis characterized by the appearance of pain in the stomach, occurring when the stomach is empty, and which disappears as soon as food is taken. It may occur as a permanent neurosis, or come on periodically. According to Boas, this condition is produced by severe contractions of the pylorus, and is relieved when food is present in the stomach.

Etiology.—This condition is found in neurasthenic individuals who are subject to worry and anxiety, or who have been leading an irregular life. Examination of the gastric functions shows normal conditions both as to secretion and motility. This affection occurred only in males in 7 of this series (0.5 per cent.); of these, 3 were between twenty and thirty, 3 between thirty and forty, and 1 between forty and fifty years.

Symptoms.—The condition manifests itself by the appearance of pain, which at times becomes intense, from one to two hours after meals. An attack may appear during the day or night, and last from fifteen to thirty minutes. The pain is immediately relieved by taking food.

Treatment.—This consists in properly looking after the underlying neurasthenia. Patients should not allow the stomach to become empty, and should be encouraged to take food every two hours. Boas obtained good results by the administration of some form of opium.

GASTRALGIA NERVOSA

Gastralgia nervosa is the condition characterized by periodic or spasmodic attacks of pain in the stomach, appearing independently of the ingestion of food and not associated with any organic disease. The pains of a gastralgic type present in ulcer, cancer, dilatation, and cannot be properly classified under this head.

Etiology.—Gastralgia is usually considered as a neurosis of the vagus, and only a marked increase in the condition to be described as gastric hyperesthesia. Einhorn divides gastralgias into five varieties: (1) Of gastric origin; (2) of central origin; (3) of neurotic origin; (4) of constitutional origin; and (5) of reflex origin.

1. Gastralgia of gastric origin. In this class are the neuralgic pains in cancer and ulcer of the stomach, in certain forms of gastritis, and produced by adhesions from the stomach to other organs.

2. Gastralgia of central origin. In this class are the attacks of pain observed in the gastric crises of locomotor ataxia, and the gastric pains in cerebral tumors and myelitis.

3. Gastralgia of neurotic origin. This occurs in hysteria and neurasthenia, and usually simultaneously with other nervous symptoms.

4. Gastralgia of constitutional origin including infections and intoxications. Gastralgia may be due to some change in the blood, as in lead-poisoning, anemia, and gout and occurs in infections, as malaria, and not uncommonly as the result of focal infections.

5. Gastralgia of reflex origin. This form is due to disease of other organs, as the generative system, enteroptosis, abdominal adhesions, biliary and renal calculi and chronic appendicitis.

Gastralgia is more frequent in women than in men. In this series of 1592 cases of gastric neuroses, there were 24 cases of gastralgia (1.5 per cent.), 17 being in females and 7 in males.

Symptoms.—The attacks of pain, as a rule, appear suddenly; occasionally they are preceded by premonitory symptoms, such as fulness in the stomach, nausea, vomiting, and headache. The pain may be burning, boring, tearing, cutting, or gnawing, and is usually felt in the epigastrium; at times it radiates throughout the entire abdomen or even to the back, and may be so intense as to cause weakness and collapse, the patient having a thready and irregular pulse, with pallor, cold extremities, and sweating. Often the pains are relieved by pressure; at times these symptoms are accompanied by nausea, vomiting, and hysterical manifestations, such as globus hystericus and nervous chills. The duration varies, the attacks may last from a few moments to many hours, and the intervals between may be days, weeks, or months. In the gastric crises of locomotor ataxia the attacks of gastralgia are usually ushered in with pains in the legs and arms, nausea and vomiting. These crises may precede the classic signs of locomotor ataxia by months or years. Boas called attention to the gastralgic pains occurring in neurasthenic females at the menstrual period.

In most instances this condition bears no relation whatever to the character of the food taken. The pains begin in the epigastrium, remain

localized, and are burning and boring in character. The attacks last from fifteen to thirty minutes, and are repeated several times during the day, while at night the pain is absent. Another form is that produced by open inguinal or femoral rings, occasioning small or occult hernia, also by hernia of the abdominal walls. These are observed most frequently along the linea alba. The pain is colicky, and ceases when the patient reclines. Neurasthenic symptoms are almost always present.

Diagnosis.—This is made by the character of the attacks with paroxysmal pain, bearing no relation to the ingestion of food, and at the same time not associated with any organic or other functional disease of the stomach. As gastralgia is usually due to some other condition, care should be taken to determine as far as possible its etiological relation. Gastralgia must be differentiated from ulcer. In *ulcer* there is a circumscribed painful area in the epigastrium and in the back to the left of the eleventh or twelfth dorsal vertebra. The pain is proportionate to the quality and quantity of food ingested, and is accompanied by nausea and vomiting; is relieved by vomiting; occult blood is found in the feces at times. When there is still doubt Leube recommends the ulcer rest cure in order to determine from the result of the treatment the presence or absence of ulcer. Gastralgia is differentiated from *chronic gastritis* by the slower appearance of the pains after the ingestion of food, by the presence of the paroxysms of pain, and by the absence of any change in the gastric secretion. It is differentiated from *cancer* by the absence of the usual signs; the pain usually not being paroxysmal in cancer. Intestinal *colic* may be mistaken for gastralgia, but in it the intestine is inflated with gas, and the pain is relieved by the passing of gas or a movement of the bowels, which frequently contains mucus. The pain of intestinal colic changes its position, while in gastralgia it is localized, as a rule, in one area. Intercostal *neuralgia* is distinguished from gastralgia by the fact that in the former condition the intercostal area is painful to pressure along the course of the nerve. *Gall-stone attacks* may be mistaken for gastralgia. In these the pain is generally to the right of the median line, the attack is accompanied by fever, and there is often a sensitiveness of the liver. In some cases the diagnosis is most difficult, especially when the more important symptoms of cholelithiasis are absent. *Nephritic colic* is differentiated from gastralgia by examination of the urine. The pain in nephritic colic radiates toward the bladder.

Treatment.—It is important to direct our attention to the underlying cause. The form due to anemia should be treated with iron and arsenic; that due to malaria by means of quinine; and that from nicotine poisoning by cautioning against the use of tobacco. Reflex gastralgia must be handled by treating the primary disease. That due to neurasthenia and hysteria should be treated by change of scene, rest, and massage. In patients much run down a systematic rest cure will produce excellent results. The attacks of pain are treated as follows: hot applications in the shape of a hot-water bag or hot poultices or packs are placed on the abdomen and the patient given half a grain (0.03 gm.) of codeine or 20 to 30 drops (1.5 cc.) of Hoffman's anodyne. Belladonna

and chloroform water have also been recommended, as well as phenanacetine and pyramidon. If the attacks of pain are intense, a hypodermic injection of morphine must be administered or opium and belladonna given by rectum. The galvanic current is of considerable value, the anode being placed on the epigastrium and the cathode on the spinal column. Strong currents are used.

HYPERESTHESIA GASTRICA

By gastric hyperesthesia is meant that condition in which the mucous membrane of the stomach is unduly sensitive, even to its normal contents. The lightest forms of foods will often cause distress in spite of the fact that the stomach presents neither secretory nor motor disturbances. The character of the discomfort may be pain, fulness, burning, or sensations of cold occurring after meals. In some instances, not only does the food cause discomfort, but the normal amount of hydrochloric acid will cause pain, similar to that found in hyperacidity, and it may exist even when the acid is diminished or absent.

Under the subjects of achylia gastrica and hyperchlorhydria, it was shown that symptoms of hyperacidity occasionally exist in achylia gastrica; in these cases there is evidently a hyperesthesia of the gastric mucous membrane, which is so sensitive that it cannot tolerate even the normal amount of acid. On the other hand, a condition is observed in which the percentage of acid may be far in excess of normal, and yet the individual have perfect health without gastric disturbance.

Etiology.—As a primary affection, hyperesthesia is found in neurasthenia and hysteria, and frequently in anemic females; it occurs secondary to affections of various organs, such as ulcer of the stomach, chronic gastritis, and disease of the kidneys (uremia). It may be produced by excesses in food and drink, the abuse of coffee, tea, alcohol, indulgence in highly seasoned food and tobacco, or it may come from drug habits, such as opium or cocaine. The taking of insufficient food, fasting, living on an exclusive diet, or eating irregularly are also etiological factors. Hyperesthesia is the affection from which conditions such as anorexia nervosa, nervous nausea and vomiting, gastralgia, and sitophobia often take their origin. In this series of 1592 cases there were 31 cases of hyperesthesia (2 per cent.).

Symptoms.—The sensation produced is that of mild pain, fulness, and burning, appearing soon after meals and continuing during digestion, and ceasing when the stomach is empty. In some cases the pain is greater, and may cause nausea and vomiting. The disturbance is often greater from liquid than from solid food. On account of the discomfort produced, much food is discarded and the patient emaciates and loses strength. Some of the cases manifest the symptoms of hyperchlorhydria, notwithstanding that the acidity may be normal or subnormal. In these cases the discomfort appears several hours after meals and disappears on the ingestion of food or the taking of alkalis. On palpation the whole gastric area may be sensitive to pressure but free from localized painful points. The gastric secretion, even following a fractional analysis,

shows a normal percentage of free acid, with occasional slight variations. The motor function of the stomach is not disturbed.

Diagnosis.—This is usually made with ease, provided the symptoms above described are present together with a normal gastric secretion. Hyperesthesia must be differentiated from ulcer and chronic gastritis. In ulcer there is a localized painful area and the pain is proportionate to the quality and quantity of food ingested. In chronic gastritis there is usually a diminution of gastric secretion, together with the presence of mucus, while the symptoms of distress do not appear immediately after meals, but some time later.

Treatment.—In all instances the patient should be required to remain in bed, at first on a milk or egg-albumen diet, and, if possible, combined with a systematic rest cure, the food being increased gradually until solid food is taken. In serious cases, rectal alimentation must be practised for a few days at the onset. Cold compresses should be applied to the abdomen. Galvanization is efficacious in some cases. Nitrate of silver may be given by mouth, grain $\frac{1}{8}$ (gm. 0.008) in solution, three times daily, or administered by means of the stomach douche. At times the bromides, valerianates, and sumbul prove useful, especially in those forms due to neurasthenia and hysteria to which attention must always be directed. In the cases dependent upon anemia, iron is indicated.

Gastric Idiosyncrasies and Abnormal Sensations.—There are certain individuals who manifest an idiosyncrasy toward certain foods which when taken produce gastro-intestinal disturbances or some eruption on the skin. Among the foods causing this class of symptoms are fish, berries, cheese, etc. Fever, headache, gastric pain, nausea, vomiting, and urticaria are accompanying symptoms. The diagnosis is often aided by means of sensitization tests. The only means of preventing it is to have the individual abstain from the food that causes this discomfort or to desensitize him. There are abnormal sensations in neurotic individuals, such as cold, heat (stomach burn), epigastric pulsations, constrictions, and sensations of a foreign body in the stomach. The gastric secretion is normal in all these instances, and there are usually other neurasthenic symptoms that indicate the nature of the disorder. The treatment must be directed to the nervous system in general. The bromides and belladonna are at times of value.

MERYCISM OR RUMINATION

By merycism is meant that condition in which there is a regurgitation of food into the mouth which is again masticated and then either reswallowed or ejected. This act is accompanied by a more or less pleasurable sensation and without nausea or effort, and occurs some time after meals. Rumination in man is comparable to the same condition found in certain animals. Some authorities attribute this disorder to a paresis of the cardia, while others consider it a reflex neurosis causing a temporary relaxation of the cardia. Rosenthal holds it is due to an irritation of the vagus, producing an opening of the cardia through Openchowski's dilator fibres, occasioning an antiperistalsis of the

œsophagus. There are two classes of phenomena aiding in the production of the disorder, one active, the other passive; the active consists in depression of the diaphragm and contraction of the muscles of the abdomen, both of which produce a void in the thoracic cavity; and contraction of the abdominal muscles which compress the stomach. "The passive phenomenon consists in the elongation and widening of the œsophagus and the diminution of the lumen of the stomach" (Spivak).

Etiology.—Heredity plays a role in a number of cases which have been reported. The writer has observed the condition in a father aged fifty-one and a daughter aged fourteen years. In many cases other neurotic and hysterical tendencies have been observed. At times the condition is acquired by imitation.

Among the causes to which rumination is said to be due are rapid eating, worry, fear, nervous strain, and sudden shock. A large number of cases occur among idiots and the insane. The disease is observed more frequently among men than women. It is found at all ages, and is most common in highly intellectual men. In the series of 1592 cases of gastric neuroses there were 24 cases of merycism (1.5 per cent.). Among them were five students, one artist, two lawyers, three physicians, five clergymen, two merchants, one baker, and one mechanic. The gastric contents were examined in 19 of the 24 cases of this series; a normal acidity existed in 11, hyperacidity in 3; subacidity in 2; anacidity in 1; and heterochylia in 2 cases. Atony was found in 3 cases, while in the others the motor function was normal.

Symptoms.—Rumination usually begins as a voluntary process in an insidious manner; on account of gastric discomfort the food is first regurgitated, producing a pleasurable sensation it is again reswallowed, and finally the condition of merycism is established as an involuntary process. The regurgitation usually takes place during the early period of gastric digestion; it rarely occurs in the fasting stomach; the remastication continues as long as the regurgitated food has a pleasant taste; as soon, however, as it becomes acid (during the late period of digestion) it is either swallowed at once or ejected. Rumination may take place after every meal and last for a very short period or extend over hours. Merycism occurs alone or may accompany other gastric disorders; it is occasionally associated with atony and dilatation of the stomach. As a rule, the general nutrition of patients with this disorder is good; although when large portions of all meals are not reswallowed emaciation is produced and the general nutrition is affected.

Diagnosis.—This is made without difficulty. It differs from regurgitation in that the food is again masticated, while in the latter this process does not take place. In vomiting, nausea and retching are present, while merycism is accompanied by pleasurable sensations.

Prognosis.—This is often good, especially if the patient makes the effort to overcome the habit. This condition may extend over a long period of time, being present occasionally during the entire life, or it frequently disappears for a period, to recur following some strain or shock.

Treatment.—This consists essentially in an autosuppression. In a certain number of cases the patient can be taught to overcome this

disease. He should be required to eat slowly and masticate thoroughly; 3 patients of this series were cured in this way. The state of the gastric secretion occasionally gives a clue as to treatment. Hydrochloric acid is useful in cases of subacidity while alkalis are of benefit in superacidity. Intragastric electricity has been recommended, and was of great benefit in 2 patients. In those who are much run down and weakened by disease a thoroughly regulated rest cure with psychotherapy is most effective; 3 patients were cured in this way. Strychnine and quinine have been recommended, inasmuch as their taste destroys the desire to remasticate. Lavage has been used by Johannessen and gavage by Jurgensen.

REGURGITATION

By regurgitation is meant that condition observed in hysterical and nervous individuals when food is brought up in small quantities from the stomach into the mouth and usually ejected. This disorder is much like rumination, except that food is not remasticated; rumination, however, may develop from long-continued regurgitation.

Etiology.—This is the same as that of rumination. The condition is usually found in neurasthenic and hysterical individuals, and is at times voluntary; however, as the habit becomes established it becomes involuntary. Regurgitation may be occasioned by a nervous strain or shock, or may be secondary to some other gastric disturbance, such as dilatation, catarrh, or hyperchlorhydria. This disorder is also largely found in adult males, and more frequently in individuals pursuing intellectual pursuits. It occurs more frequently than rumination. In the series of 1592 cases of gastric neuroses it was present in 32 cases (2 per cent.), 26 being in males and 6 in females. Among those suffering from this affection, there were two artists, three students, three physicians, six lawyers, five ministers, four teachers, three merchants, one mechanic, and one laborer. The gastric secretion is usually normal. In the series of 32 cases the gastric contents were examined in 29, and normal acidity was found in 23 (79 per cent.), hyperacidity in 3 (10 per cent.), subacidity in 2 (8 per cent.), and heterochylia in 1 (3 per cent.). The motor function was usually normal, a slight atony existing in five.

Symptoms.—The onset is gradual, and consists in the regurgitation of food from the stomach soon after eating and persisting during the entire period of digestion. It is not preceded or accompanied by nausea, and if it occurs early in the process of digestion, the regurgitated material has the same taste as the food swallowed. Later it becomes sour from the mixture of the acid of the gastric juice. At times this process can be suppressed, at other times not. The food is not remasticated and swallowed with pleasure, as in the cases of rumination. Regurgitation may occur after any meal, or only after certain ones; it may disappear for a time, to recur after some mental strain or excitement. When large portions of all meals are habitually regurgitated and ejected, the general nutrition of the patient is likely to suffer.

Diagnosis.—Regurgitation is differentiated from vomiting by the absence of the usual signs of the latter, nausea, retching, salivation, etc.

It is distinguished from œsophageal regurgitation due to stenosis of the œsophagus by the presence of the gastric secretion in the regurgitated matter. The difficulty or inability to pass the tube in œsophageal stenosis aids in differentiating this from gastric regurgitation.

Prognosis.—This is usually favorable, provided the patient will assist in the act of suppression of the condition; the health becomes seriously affected only in those instances in which all food is constantly regurgitated.

Treatment.—The general condition should be looked into and the associated neurasthenia or hysteria treated. An important factor consists in teaching the patient voluntary suppression. In emaciated individuals this may be assisted by a rest cure with isolation. The patient should be required to eat slowly and masticate his food thoroughly. Strychnine and the bromides have been used with good results.

ERUCTATIO NERVOSA OR AËROPHAGIA

Eructatio nervosa is a condition characterized by periodic or paroxysmal attacks of noisy belching; it occurs in neurasthenic and hysterical individuals. The question of the origin of the gas expelled has attracted much attention. The following sources have been suggested: The fermentation or putrefaction of food, causing the formation of gases, or the swallowing of air (aërophagia). It is now generally admitted that the gas which is expelled in eructatio nervosa is swallowed, and that the air passes into the stomach by an act of deglutition. The swallowing of small quantities of air is a natural phenomenon accompanying the deglutition of food. Aërophagia, on the other hand, occurs as a voluntary act, induced to relieve an uncomfortable sensation in the stomach or œsophagus by the expulsion of gas that has been swallowed. Convulsive deglutition is accompanied by forcing air into the œsophagus and stomach, while expulsion is occasioned by contraction of the œsophagus expelling the accumulated air with a loud characteristic sound. Oser[1] ascribes this condition to aspiration, air being suctioned in and expelled through the œsophagus by expansion and contraction of the stomach. Linnosier believes that aërophagia is much like regurgitation, and that while in regurgitation there is an expulsion of food, in aërophagia there is an expulsion of gas. In some cases, as Ewald points out, the belching has no connection with the stomach, but originates from the œsophagus by contractions of the muscles of the neck.

Etiology.—Eructatio nervosa is usually found in hysterical or neurasthenic individuals. It is more common in females, and in younger than in older persons. In the series of 1592 cases of gastric neuroses there were 54 cases of eructatio nervosa (4 per cent.), 42 in females and 12 in males. While this condition is usually a simple gastric neurosis produced by some mental excitement, such as anger, worry, or great sorrow, yet it may occur as a result of some other gastric disturbance. Catarrh, gastroptosis, or a reflex condition secondary to disturbances of other organs, such as the genito-urinary organs and heart, may produce it.

[1] *Die Neurosen des Magens*, 1885, S. 137.

Symptoms.—This disorder usually develops suddenly and is accompanied by noisy eructations, which vary in duration and intensity, the paroxysm lasting from a few hours to days. Frequently there is a period of quiescence between the paroxysms, the attack presenting no definite relation to the quality and quantity of food taken. The number of eructations varies greatly. Spivak calls attention to two forms of nervous eructations, voluntary and involuntary. In the first variety the patient controls the condition, and is able to inhibit this habit at will; in the second, which generally occurs during an attack of hysteria, he is unable to do so. The attack is spasmodic in character and cannot be controlled. The paroxysm usually disappears suddenly and ceases during sleep. On examination, patients suffering with nervous eructations present a rather increased sensibility to pressure in the epigastric region. These areas on pressure occasion eructations (aërophagenic points, Bandouin). Examination of the gastric contents may or may not reveal normal conditions. In this series of 54 cases the gastric contents were examined in 51; normal acidity existed in 42 cases (82 per cent.), superacidity in 6 (12 per cent.), and subacidity in 3 (6 per cent.).

Diagnosis.—This is not usually difficult. The characteristic paroxysmal attacks can scarcely be mistaken. There is usually an absence of organic disease; the gastric contents are frequently normal (82 per cent. of this series); the gas expelled is atmospheric air and shows no signs of fermentation, while the examination usually reveals other neurasthenic or hysterical symptoms.

Treatment.—Mild forms of the disorder may be combated by explaining its nature to the patient and urging him to control the attack. Sometimes, however, this is difficult, and we must content ourselves with the treatment of the neurasthenic condition. This may be accomplished by hydrotherapeutic measures and change of scene. In persons who are much run down and have lost much flesh nothing will accomplish such excellent results as a well-regulated rest cure. In those instances in which the eructations are violent and continuous it has been advised that the mouth be kept open by placing a cork between the teeth. By means of this the eructations are prevented, as the patient is unable under this condition to swallow air. At times good results may be obtained by lavage, douching the stomach, or by intragastric electricity. Drugs are usually of little value. Among those employed in this condition with more or less effect are the bromides, chloral, codeine, and belladonna.

NERVOUS VOMITING (VOMITUS NERVOSUS)

The act of vomiting is a very complicated process; not only does the nervous system play a part in the act, but also the muscles that govern the movements of the stomach. In addition to the centres governing the stomach movements there is a coördinated action of the vomiting centre from which this act takes it origin. The vomiting centre is in the medulla in the vagus nucleus in close proximity to the centres transmitting impulses to the muscles of the stomach, diaphragm, and pharynx.

Etiology.—Vomiting may be due to one of three conditions: to some abnormal state of the food, to some disease of the stomach itself, or to some disturbance of the nervous system. The form with which we are here concerned comes under the latter head. It may be divided into three groups: (1) Cerebrospinal vomiting due to a lesion or functional disturbance of the nervous centres. (2) Nervous vomiting proper, or vomiting due to neurasthenic or hysteria. (3) Reflex vomiting.

Stiller[1] points out the following features as characteristic of this form: (*a*) The ease of the vomiting. (*b*) Its non-dependence upon the quality and quantity of the ingested food. (*c*) The capriciousness with which very bizarre articles of food are retained to the exclusion of others. (*d*) The occasional elective vomiting that consists in selecting only one form of food which is separated from the chyme. (*e*) The ease with which patients bear this condition even for a long period of time. (*f*) The very slight degree of inanition produced by the habitual vomiting. (*g*) The extraordinary influence of the slightest external or internal causes that react on the patient's temperament. (*h*) The occurrence of vomiting frequently, even on a fasting stomach, and the appearance of this condition independently of the meal. (*i*) The presence of other nervous symptoms associated with the vomiting or alternating with it.

In this series of 1592 cases of gastric neuroses there were 49 of nervous vomiting (3 per cent.), 34 in females and 15 in males; as to age, 6 were in the first decade, 6 in the second, 14 in the third, 11 in the fourth 8 in the fifth, 3 in the sixth, and 1 in the seventh.

1. **Cerebrospinal Vomiting.**—The cause of this form (also known as central vomiting) is found in the brain, spinal cord, or the membranes covering these structures. The condition has been observed as a symptom of inflammatory disease of these structures. It is found in meningitis, encephalitis, apoplexy, abscess, cerebral tumors, not infrequently after brain anemia or hyperemia, concussion, intoxication from ether. chloroform, opium, tobacco, or septicemia and auto-intoxication. Spinal vomiting due to disease of the cord is rather infrequent; it occurs most commonly in the gastric crises of locomotor ataxia and occasionally in transverse myelitis. The *gastric crises* are characterized by the occurrence in the midst of well-being, of sudden attacks of intense pain appearing in the epigastrium radiating toward the sides and back. They are followed by the vomiting of large quantities of food, mucus, bile, and finally of intestinal juices and occasionally of blood. After copious vomiting temporary relief is afforded, and the attack ceases, especially during the night, to return on the following day. It may continue at intervals from six to eight days, or may last even longer. The vomiting may cease as suddenly as it appeared, the appetite may return, and the general condition of the patient improve.

During an attack the patient becomes weak and prostrated, the pulse is feeble and rapid, the appetite disappears, the bowels become constipated and the thirst intense, while the abdomen is much retracted. The examination of the vomited matter for free hydrochloric acid may

[1] *Die nervose Magenkrank*, 1884, S. 151.

reveal a normal, subnormal, or hyperacid secretion. The diagnosis of locomotor ataxia is made by the presence of the other characteristics of this disease, but inasmuch as gastric crises may occur as early symptoms of tabes, the diagnosis may be difficult.

2. **Nervous Vomiting Proper.**—This form of nervous vomiting is most frequently associated with neurasthenia or hysteria. It is found mainly in hysterical females; in this series it occurred in 19 females to 4 males. The vomiting is often accompanied by pains in the stomach, and comes on more or less frequently every day or every few days and is often observed after some severe mental strain or excitement. Nausea is frequently absent in these cases, the vomiting occurring without any effort whatever; other symptoms of neurasthenia or hysteria are either associated with the vomiting or alternate with it. The *diagnosis* of nervous vomiting is established by the presence of associated nervous symptoms, and by its non-dependence on the quantity and quality of food taken; further by its irregularity, the expulsion of either only solids, or only liquids, or only one particular form of food, or only a portion of the meal, and the very slight loss in strength and weight. In this condition the skin is usually dry; the quantity of urine excreted is small, with a marked diminution in urea. The vomiting may continue for days or months and then disappear suddenly without apparent cause.

Periodical Vomiting.—This condition was first described by von Leyden, and is characterized by vomiting occurring at regular intervals; between the attacks the patient is in normal health, and complains neither of gastric distress nor disturbance of the nervous system. The attacks come on abruptly and disappear as suddenly, lasting from a few hours to twelve or fourteen days, the attack as well as the interval having a constant and definite duration. The attack is usually ushered in abruptly by nausea, gastralgic pain, and headache, followed by vomiting, at first of gastric contents and mucus, and then of bile. The vomiting is excessive, no food, not even fluids, being retained by the stomach during this period. The patient becomes weakened and prostrated, the pulse weak, the tongue dry, severe, lancinating pains often occur in the extremities, constipation becomes marked, and the urine is diminished. The vomiting ceases suddenly and the attack gradually passes off, to be repeated again at an interval of from two to four or six weeks or even several months. When the attacks occur at short intervals emaciation may be extreme, and the disease becomes most serious, in consequence of the extreme inanition produced. A distinctive feature is the typical periodicity by which it can be distinguished from the gastric crises of tabes. An examination of the stomach contents in these cases usually reveals normal conditions.

Psychic Vomiting.—This is generally due to some form of shock, fright, or sudden mishap. It may be mild or intense. In mild forms only portions of the food are vomited for a certain period of time, and the attack then disappears, the general nutrition not being markedly impaired; in the severe form the inanition may be so great that the disease may become extremely serious, or even fatal.

Juvenile Vomiting.—This form occurs in children who have been subjected to overstudy. In addition to the vomiting, other symptoms, as a rule, present themselves. The disorder usually begins with gastric pains and vomiting, to which such symptoms as headache, pallor, dilated pupils, a slowing of the pulse, and constipation are added. Improvement usually follows when the patient discontinues his school work.

Periodic Vomiting in Children.—A peculiar form of periodic vomiting, differing from the form described as juvenile vomiting, occurs in young children. It comes on usually at the age of from two to three years, and generally passes off as the child becomes a few years older. The attack is characterized by a sudden onset of intense vomiting, accompanied by fever and great depression, that ceases as suddenly as it began. In a certain number of cases the attacks appear with a distinct periodicity at intervals of a few weeks or even months. In at least some there is an intermittent hyperchlorhydria. In some cases the condition is associated with acidosis.

3. **Reflex Vomiting.**—This is a very common form of nervous vomiting, and may be produced by various diseases affecting the stomach and other organs. It is found as one of the symptoms of disease of the middle ear, disturbances of the eye, pharynx, larynx and tonsils. To these may be added diseases of the lungs and abdominal organs. Reflex vomiting is also common during pregnancy.

Gould and others have pointed out the frequent dependence of this as well as other gastric neuroses upon eye-strain, while Brav has found astigmatism a common cause of vomiting in school children. The vomiting of pregnancy is often a reflex neurosis of the sympathetic nerves. In another form vomiting is due to some hysterical or neurasthenic tendency. In these cases the neurotic nature is indicated by the fact that a cure frequently follows the employment of perfectly useless and unphysiological procedures. Many of these cases, therefore, may be cured by rest or simple suggestive means. A third variety of vomiting of pregnancy is the toxemic form, which is a very serious disease and is produced by a marked disturbance of metabolism with a resultant toxemia.

Diagnosis.—The diagnosis between the various forms of nervous vomiting is not always a simple matter. After establishing the nervous origin of the vomiting it is most important to determine its exact cause, whether, for example, it is reflex or due purely to neurasthenia. These facts, as a rule, can be elicited by a complete investigation into the history and a rigid examination of the patient.

Prognosis.—This depends largely upon the cause. In the cerebrospinal vomiting it is usually bad, although in the gastric crises the vomiting may abate entirely, notwithstanding the continued progress of the disease. In the form with neurasthenia or hysteria the prognosis is usually favorable when under proper treatment, but occasionally a fatal outcome is met with, due to exhaustion occasioned by the continued and prolonged vomiting. Three cases of this character have come under the observation of the writer. In the reflex form the prognosis is favorable provided the cause can be removed.

Treatment.—The chief aim is removal of the cause. Inasmuch as this is not always possible, many patients must be treated symptomatically. In the milder forms, change of scene, avoidance of mental excitement, and rest will overcome this condition. In severe cases patients should always be placed in bed in a hospital under rigid isolation and rest-cure treatment. In seven of this series the writer is convinced that the lives of the patients were saved by this plan of treatment.

As regards diet, the patient should be given liquids in very small quantities, such as champagne, ice-cold milk, clam broth, or cold egg-albumen. In severe forms the patient must be fed for some days by the rectum and the thirst relieved by saline enemata. Duodenal alimentation by a duodenal tube has proved highly efficacious in many cases under the writer's care. In some cases solid foods are well borne when liquids cannot be taken. These should be given in very small quantities; scraped beef, eggs, rice, and toast are especially useful. Hydrotherapy may be practised with good results in some cases. Electricity has a beneficial effect in some instances, the galvanic current being used with the anode in the stomach and the cathode on the spinal column. The writer has had good results at times from lavage with solutions of nitrate of silver, at other times with solutions of menthol. As to the drugs used with more or less effect the following may be mentioned: Morphine given hypodermically, oxalate of cerium, cocaine, menthol, the bromides, chloral, validol, and orthoform. Suppositories of opium and belladonna are useful in attacks of periodic vomiting. In the periodic vomiting of children Rachford suggested the use of calomel and bicarbonate of soda, followed by a saline laxative, and then benzoate of soda in from 3 to 8 gr. (0.2 to 0.5 gm.) doses every two or three hours.

NAUSEA NERVOSA

Nausea is observed in many gastric affections, as well as in diseases of other organs. There is, however, a purely functional form of nausea which is entirely of nervous origin and is due to hysteria or neurasthenia.

Etiology.—Nausea nervosa is often found in anemic and chlorotic females; it is also observed with menstrual disturbances and frequently at the menopause. It begins, as a rule, after great excitement, worry, or anxiety in neurasthenic or hysterical individuals. This disorder is most often observed in women and rarely in men. In the series of 1592 cases of gastric neuroses there were 40 cases of nausea nervosa (2.5 per cent.), 30 in females and 10 in males. As to age, 13 were in the second decade, 9 in the third, 7 in the fourth, 7 in the fifth, and 1 in the sixth.

Symptoms.—Nausea may be intermittent or continuous. In the intermittent form it appears any time of the day or night and bears no relation to the ingestion of food, its quantity or quality. In the continuous form it persists for days and months in varying degrees of severity, sometimes slight, at other times so intense as to cause vomiting. The nausea is not dependent upon the quantity or quality of the food ingested, yet it causes a loss of appetite, and the patients, as a rule, live upon a very limited diet, the result being great emaciation. Examination of the

gastric contents showed a normal acidity in 34 and in 6 a hyperacidity. The gastric motility was normal in all.

Diagnosis.—All organic diseases accompanied by nausea must be excluded, such as tuberculosis, diseases of the genital organs, arteriosclerosis, uremia, and organic diseases of the stomach.

Treatment.—In many cases due to anemia or chlorosis appropriate treatment will relieve the condition. Attention should be paid to repair of the nervous system, especially by massage, electricity, and hydrotherapy. In those cases accompanied by marked anemia and great loss of flesh splendid results are obtained through a well-conducted rest cure. Complete isolation is always necessary in severe forms. Duodenal feeding may be practised at times with advantage. Relief is shown in some cases by means of the bromides, valerian, sumbul, and chloral. Validol for milder forms has been of great service in the writer's experience.

CARDIOSPASM

Spasm at the cardia and cardiospasm are terms which have been used more or less synonymously to denote a spastic affection of the lower area of the œsophagus. Much confusion exists in the literature regarding the nomenclature of these affections, and Smithies has again called attention to the fact that the two conditions must be distinguished from each other. In spasm at the cardia a temporary contraction occurs, which is transient in character; whereas in cardiospasm, in addition to hypertrophy or an unusually strong and prolonged contraction of the cardia, a diffuse dilatation of the œsophagus is also produced. Most observers consider spasm at the cardia as an acute stage always preceding the chronic lesion of cardiospasm.

Etiology.—The etiology of cardiospasm and diffuse dilatation of the œsophagus has been a matter of dispute. A few suggested factors may be noted: Rosenstein considers the primary condition to be an atony of the musculature of the œsophagus with secondary spasm of the cardia. Kraus believes that the condition is due to the simultaneous development of a prolonged spasm at the cardia and a paralysis of the circular muscles of the gullet brought about by degenerative changes in the vagi. Some observers maintain that a congenital predisposition is responsible. Martin considers a primary œsophagitis to be an important factor; and such conditions as congenital or acquired asthenia, organic lesions of the stomach and œsophagus such as ulcer or cancer and kinking of the œsophagus at the cardia are among other explanations offered. Chevalier Jackson has shown that in some cases the œsophagus is "pinched" where it passes through the diaphragm.

Mikulicz, Meltzer and Plummer believe that in addition to changes at the cardiac sphincter, there exists some disturbance of the neuromuscular mechanism of the œsophagus which may permit diffuse dilatation irrespective of actual stenosis due to hypertrophy of the cardiac sphincter. Plummer calls attention to the fact that some individuals exhibit a habit spasm at the cardia without any dilatation of the œsophagus. Smithies believes that there always exists a definite hypertrophy

of the muscular cardiac ring with demonstrable generalized dilatation of the œsophagus of varying degree in cases of cardiospasm. Aaron's explanation of this condition seems plausible. According to him, under normal conditions the cardiac sphincter contracts and relaxes, due to the action of stimuli carried respectively through the vagus and sympathetic nerves. Only the initial act of swallowing is voluntary, while the balance of deglutition is a complicated reflex act in which the peristaltic wave follows the bolus of food, the gullet contracting above and relaxing below the food. During each act of swallowing, inhibitory impulses pass from the sympathetic to the cardia causing the latter to relax and receive the bolus of food. In cardiospasm this inhibitory control is apparently absent, so that the cardia remains in a state of continuous contraction, producing a muscular hypertrophy by overwork at the cardia, and later a diffuse dilatation of the œsophagus. This disturbance in the normal mechanism may be of central, reflex or intra-œsophageal origin. Thus shock, worry and trauma with the hurried gulping of food may be among the contributing factors concerned. It is interesting to note that spasm at the cardia is not uncommonly produced reflexly, by disease of organs elsewhere, as by infections of the gall-bladder or appendix, lesions of the stomach, duodenum, and œsophagus, or abdominal adhesions, and on the other hand, it may be accompanied by spasm elsewhere (pylorospasm). Notwithstanding the removal of the primary affection, the spasm may persist and finally lead to a true cardiospasm. Attention must be directed to a small group of cases of spasm at the cardia first noted by Plummer and more recently by Vinson in which in addition to the dysphagia, a secondary anemia with enlargement of the spleen develops which disappears when deglutition again becomes normal. Cardiospasm also at times accompanies hysteria and neurasthenia.

Spasm of the cardia occurs most commonly in young adult life between the ages of eighteen and thirty years. Cardiospasm is more frequent in mid-adult life between the ages of twenty-five and fifty years. Cases have been recorded varying in age from four to eighty-three years. Smithies and Plummer observe no difference as to its occurrence in the two sexes; Verbrycke finds 61 females and 39 males affected in his series. Our experience would indicate that sex plays only a minor role and although spasm of the cardia occurs more frequently in females, cardiospasm is as prevalent in males as in females, since all cases of the former do not develop dilatation.

Symptoms.—Plummer describes three stages: (1) Spasm at the cardia in which the œsophageal muscle is able to overcome the resistance at the cardia; (2) in which a relative or actual increase in the spasm occurs so that the peristaltic action of the œsophagus is not sufficient to force food through the cardia; and (3) a stage characterized by the formation of true cardiospasm with diffuse dilatation. These stages necessarily overlap, and the symptoms depend upon the stage of the disease at hand. Spasm of the cardia, which may be considered the acute form, comes on suddenly following an emotional upset or after the hurried gulping of food and at times even without any attributable cause. The attack is accompanied by a choking sensation, discomfort and burn-

ing in the substernal region and at times by dysphagia. This condition may last a few hours or days and periods of well being may alternate with exacerbations. After a variable period of time, the spasm becomes more chronic, food is forced through the cardia with great difficulty so that regurgitation becomes a prominent symptom and dysphagia is more marked. In many cases the regurgitation is of the explosive type. Some patients complain that food lodges in the chest, and only by repeated swallowing efforts or by the drinking of water can it be propelled into the stomach. After a variable period of time dilatation develops and considerable quantities of food may be retained. In one of our cases the œsophageal capacity was 2000 cc. The dysphagia which becomes more and more annoying is not always painful. Some patients complain of dyspnœa, cough, crowding of the heart, palpitation and angina-like pains. Liquids are more prone to produce immediate distress than solids, although some patients have as much difficulty in swallowing solids as liquids. The regurgitation in this stage occurs immediately after the ingestion of food or may be delayed for some hours. The liquid portion of a meal may pass through the cardia, and the solid food with mucus may be regurgitated or remain in the œsophagus for days. The regurgitated material does not contain any free hydrochloric acid, is alkaline in reaction, frothy, and contains much mucus. Nocturnal emesis may occur which may prevent proper rest. Other symptoms are loss of weight due to the malnutrition, anorexia, constipation, eructations, headaches, dizziness, nausea, weakness, etc. The duration of all symptoms in our series varied from a few months to many years.

Diagnosis.—The diagnosis of spasm at the cardia is readily arrived at by noting the appearance of varying degrees of dysphagia, discomfort beneath the sternum, and a choking sensation present in a neurotic individual. In some instances a definite resistance may be encountered at the cardia on passing a stomach tube or a bougie, the resistance being less perceptible to a large calibre bougie than a small one. This sign is more marked in the second stage of the disease. The periodicity in the occurrence of the attacks and the appearance of regurgitation are also suggestive symptoms. A fluoroscopic examination aids much in the diagnosis as a momentary arrest of bismuth will be noted at the cardia. When dilatation occurs the diagnosis is based on the following findings: (1) The clinical history of the preceding stages; (2) attacks of regurgitation (sometimes projectile in type) of stagnant food remains containing mucus; (3) dysphagia; and (4) the absence of the second deglutition sound. If a stomach tube is passed into the œsophagus, food remains will usually be regurgitated through and around the tube. If the bougie or tube is unguided, it may impinge upon the pendulous œsophageal sac in its lowest part; and if the bougie is passed over a thread as a guide, resistance is experienced at the cardia.

By the fluoroscope the opaque meal may be observed at first to be arrested at the cardia, then a small amount trickles through and finally the œsophagus will slowly fill, revealing a uniform dilatation, the outline of which is smooth and regular.

Einhorn devised a delineator string that casts a definite shadow on the

fluoroscopic screen or on the plates, which may be of considerable value in the diagnosis of cardiospasm. The apparatus consists of very fine copper wire (60 in a single strand) covered with braided silk, a metal ball being attached to one end of the string. The strand of wire offers no resistance to spastic movements of the œsophagus. Under the roentgen-ray, the shadow of the string appears more or less tortuous, according to the degree of the spasticity. Alterations in the outline of the œsophagus from time to time can be easily recognized by the roentgen-ray in cases of cardiospasm. After the delineator has been introduced, it may be allowed to remain, which avoids the necessity of the repeated ingestion of barium in the roentgen-ray study of this affection.

In the differential diagnosis it is only necessary to distinguish cardiospasm from carcinoma. In *carcinoma* of the œsophagus the duration of the symptoms is shorter, and the patients are usually older. Solids produce more discomfort than liquids, small bougies pass more readily than larger ones, and often carcinomatous particles, pus and traces of blood are obtained by means of the bougie. The fluoroscope shows an irregularly dilated œsophagus with a tortuous filling defect, and by the esophagoscope the ulcerated growth may be visualized and particles of the tumor may be directly obtained for pathological examination. Luetic stricture can usually be ruled out by the Wassermann test, which should be made as a routine in all patients with œsophageal stricture.

Prognosis.—In but few instances have absolute cures been demonstrated in which the dilated œsophagus returned to normal size. As a rule, when dilatation once occurs, irreparable damage is done to the œsophagus, which never again returns to a normal state although the patient may be entirely free of symptoms; however, in the early and less severe forms complete cures are unquestionably obtained. According to Smithies, clinical and functional recovery takes place in 70 per cent., improvement in 20 per cent. and 10 per cent. are not benefited by any form of treatment. Gastrostomy is necessary to prolong life in these last cases.

Treatment.—In the acute form attention should be especially directed toward the nervous system and the general health. In selected cases, rest cures, change of scene and the removal of all irritating influences prove most helpful. Large bougies should be introduced into the œsophagus and allowed to remain for a few minutes at a time if possible. A bland non-irritating diet is indicated. Bromides, valerian, belladonna, benzyl benzoate, olive oil and hyoscyamus may be administered with a variable degree of success. To prevent the occurrence of the more chronic form, that is, cardiospasm, we cannot urge too strongly the early diagnosis of spasm at the cardia. Cardiospasm associated with diffuse dilatation is an example of a more or less serious organic lesion which has its inception primarily in a functional spastic condition of the cardia.

The treatment of *cardiospasm* may be divided into two forms; those cases in which a silk thread becomes necessary as a guide for the passage of the bougie and those in which the cardia can be entered without a guide. In the milder cases, in which dilatation is only moderate and the cardia is on a line with the axis of the œsophagus, we have used the Meyer

dilator, unguided, with very satisfactory results. This dilator consists of a double rubber bag made of Penrose rubber drainage tubing between which is inserted a silk bag $1\frac{1}{4}$ inches in diameter. These three layers extending 6 inches up from the closed end of an ordinary stomach tube are securely tied at each end with silk threads. To facilitate the passage of the dilator a flexible steel wire may be used and removed when the cardia has been passed. By means of a glass syringe of 150 cc. capacity, which is connected to the mouth end of the stomach tube, the rubber bag is distended with water, over-stretching being prevented by the limitation of the silk bag. The treatments can be given at first daily, then on alternate days and the interval may be gradually lengthened to a single dilatation a month. Subsequent to a course of dilatation by this method, œsophageal bougies may be used with satisfactory results.

In more advanced cases with marked dilatation and a pouch-like formation at the lowest part of the œsophagus which may be several inches below the level of the cardia, it is impossible to force a bougie through the cardia without a guide. Mixter of Boston, called attention to the fact that a silk thread will pass through any orifice that water will pass, and Plummer utilized this method clinically in the treatment of cardiospasm. Six yards of a braided silk thread are swallowed and after several coils of the intestine have been passed the proximal end can be pulled taut without the possibility of withdrawing the thread. A perforated olive tip of a Plummer dilator is passed over the thread and by traction on the silk, the sound is directed to the sphincter and by moderate force slipped through the cardia. It is extremely dangerous to use great force in œsophageal instrumentation without a guide, as perforation of the œsophagus may occur. To facilitate the passage of the thread, lavage of the œsophagus should be thoroughly practised and belladonna administered for a few days prior to undertaking this procedure. The cardia may be dilated after being visualized through the œsophagoscope, after which the olive tips could be properly directed. The size of the olives passed are gradually increased and later on the Meyer dilator can be employed to augment dilatation. Plummer utilizes a rubber dilator similar to Meyer's with the exception that the former is passed over a string as a guide. After the dilator is in place dilatation is produced by a hydrostatic pressure of 675 mm. of Hg. Two or three such treatments are given and the patient is instructed to return if any further dysphagia is noticed.

In some aggravated forms of cardiospasm, inanition may be so great that it may become necessary to perform gastrostomy to feed the patient while dilatation is being practised from above.

An advance has been made in the treatment of strictures of the œsophagus as well as of cardiospasm by heat hyperemia, advised by L. W. Dean. According to this observer, by means of bougies heated to 45° C., the tissue is so softened that the spasm or stricture may be overcome with little difficulty.

PYLOROSPASM

By pylorospasm is meant a spasmatic contraction of the pylorus. In this affection we possess another evidence of vagatonia, inasmuch as this

condition may be produced experimentally by stimulation of the vagus and inhibited by stimulation of the splanchnics. The same condition can also be brought about by injecting certain extracts of the thyroid, parathyroids or pyloric mucosa into animals. This effect can be inhibited by atropine as well as by the injection of an extract of the adrenal glands.

Etiology.—Pylorospasm may exist in various forms, the neurotic, the irritative and the reflex. As a pure neurosis pylorospasm is rather uncommon, occurring, according to our experience, in but a small percentage of all gastric affections. In a large percentage of cases, pylorospasm is secondary to some irritation in the stomach itself or is a reflex condition due to disease of some other organ. That there are cases of pylorospasm purely neurotic in origin, there can be but little doubt. Instances of this form have been observed in infants. The purely neurotic form of pylorospasm occurs more frequently in females than in males. In our series 3 females were affected to 1 male.

While pylorospasm does not occur frequently as a pure neurosis it is quite commonly observed secondary to some gastric or abdominal affection, as gastric or duodenal ulcer, cancer of the pylorus, enteroptosis, gall-bladder disease, appendicitis, renal disorders and diseases of the male and female genito-urinary organs. The fact that pylorospasm may result reflexly from disease of other organs is clearly revealed in the gastric upsets which occur so frequently as a result of acute appendicitis or nephritic colic. By pressure on McBurney's point, Aaron was able in some instances of chronic appendicitis to produce gastric pain, and by the fluoroscope he was able to note spasm of the pylorus at the same time.

Symptoms.—The symptoms vary in intensity according to the degree of the spasm. With a moderate spasm a mild discomfort and pressure are experienced in the epigastrium. This occurs about two or three hours after meals and is usually accompanied by acid eructations and regurgitation. The pains are of the hunger type and are due, according to the researches of Carlson, Hamburger and others, to active contractions of the stomach. When the symptoms become more intense the pylorus suddenly contracts spasmodically, causing severe pain which may be followed by vomiting. The pain is usually in the epigastrium, radiating from the median line often into the back. At first the spasm appears periodically, but as the disorder progresses it may become continuous and lead to a spastic contraction at the pylorus, with consequent functional obstruction and retention of food. The food is vomited and presents all of the characteristics ordinarily observed in dilatation of the stomach. Relief is afforded for a time by vomiting, the period varying from one to four days, when a similar attack recurs. Relief is also usually obtained by emptying the stomach by lavage. After a long persistence of the affection other symptoms ordinarily observed in dilatation begin to appear, *i. e.*, emaciation, thirst, and constipation. The vomiting may be persistent, finally terminating in the expulsion of a watery mucus, very acid and containing at times streaks of blood. The vomiting is often explosive in character, the stomach emptying itself suddenly of large quantities of acid contents. As soon as the spasm relaxes the symptoms disappear.

On examination during the attack the pyloric area is tender to pressure

and contraction may take place near the pylorus, producing a firm mass, easily detected on palpation in patients with thin abdominal walls. This gradually disappears as the spasm relaxes. At this time the abdomen is rather contracted and the muscles tense. After the spasm disappears the tenderness is less and the abdomen regains its normal appearance.

The *gastric contents* may show a varying degree of acidity, depending largely upon the time when the secretion is removed. During the period of spasm there may be a lowered, normal or hyperacid content, varying according to the intensity of the attack and the time of the onset of the cramps. In the interval between attacks the gastric contents may be normal. There is usually present, however, a hyperacidity or hypersecretion, the degree of which usually depends largely upon the duration of the affection. It is rather unusual not be to able to demonstrate hyperchlorhydria some time during the digestive period by fractional analysis. After long persistence of this disorder, when obstruction with stagnation has occurred, the gastric contents assume the appearance of that observed in dilatation of the stomach.

The greatest aid in the recognition of pylorospasm is afforded by roentgenology. Both the nervous and the organic forms can usually be readily determined. Spasm of the pylorus may be determined fluoroscopically or by a series of plates, best by a combination of both methods.

It is important to determine whether the lesion producing the spasm is within the stomach or elsewhere, whether or not it is of purely nervous origin.

When spasm of the pylorus is produced by an ulcer a six-hour retention is usually present, together with a definite and persistent filling defect in the stomach, though in a number of instances in our experience the spasm and retention were the only signs pointing to ulcer. These signs may occur with ulceration in the stomach even when situated at some distance from the pylorus. The retention so constantly observed has been attributed to various conditions; it has been ascribed to pyloric spasticity due to the hyperchlorhydria, to gastric atony and to interference with the peristalsis due to the ulcer or possibly to a reflex pylorospasm.

Pylorospasm is frequently of reflex origin, not uncommonly associated with cholecystitis or chronic appendicitis. In this condition the bismuth meals are retained at the pylorus for some time; the spasm relaxes to a degree and a part or all of the bismuth is finally expelled. In some instances the spasm is so persistent that it makes one suspect an ulcer, but in a number of instances of this character under our care the diagnosis of cholelithiasis or appendicitis was confirmed by operation. *Cancer* of the stomach is at times, although rarely, accompanied by spasm; especially is this the case in the early stages of the disease or in those instances in which there is obstruction. Ordinarily, however, there is hypermotility with rapid evacuation of contents without spasm.

Diagnosis.—It is important to differentiate pylorospasm due to disease in the stomach or duodenum from that due to conditions elsewhere. Spasm due to ulcer or cancer is usually observed situated near the lesion itself and often in the area opposite to the lesion. Its location is constant

and unvarying and the spasm is definitely present throughout the entire examination as well as at subsequent examinations. The spasm caused by disease of remote organs is usually short in duration, intermittent in character and not always constant. In some instances the spasm is located at the pylorus, at others some distance from the pylorus (gastrospasm). Though usually present in the same area it changes now and then. In these instances a six-hour retention is often found at one examination and not at another. The differential diagnosis is not always certain, and it may be impossible in many instances to differentiate between the two conditions. A test to exclude pyloric spasm of nervous or reflex origin is the administration of atropine or belladonna in full doses. Spasms produced by lesions of the stomach are not influenced by this drug. Those of nervous or reflex origin usually disappear. It is interesting to note that pylorospasm, no matter whether due to disturbance within the stomach or without, disappears under narcosis, and it is for this reason that it frequently remains undetected at operation.

As a rule the diagnosis of pylorospasm is not difficult, but to distinguish those forms purely neurotic in character from those due to intrinsic or extrinsic causes is at times a most difficult problem. All organic conditions must be excluded. A correct conclusion may usually be obtained by noting the attacks of pain two or three hours after meals, which are relieved temporarily by the ingestion of food (hunger pains); in addition a tender area is usually present in the region of the pylorus; there are symptoms of hyperacidity and of intermittent stagnation; and at times a definite resistance is detected on palpation in the region of the pylorus, assuming the character of a small tumor which gradually disappears. The roentgen-ray signs are usually distinctive.

Treatment. In the treatment it should be remembered that this condition is frequently secondary to some other affection within or without the stomach, and that the primary disorder should, as far as possible, be overcome before treatment is directed to the spasm. The treatment consists primarily in properly overcoming the underlying neurasthenia. On this account change of scene, massage, rest or even a rest-cure may be found advisable. The diet should be carefully regulated; all irritating food should be avoided and the meals should be small, easily digested and given at regular intervals. In certain instances an ulcer cure with the patient in bed for two or three weeks has afforded satisfactory results. In other instances the administration of olive oil has been of great service. During the attack the best results are obtained by hypodermic injections of morphine with atropine for the pain; codeine with belladonna is serviceable. Sodium bromide with chloral has been recommended in some instances; hot applications to the abdomen and a thorough lavage with plain water, permanganate of potash or nitrate of silver solution have proved serviceable at times. The drug which is most helpful is atropine in full doses and best administered hypodermically. This drug inhibits the vagotonic irritation and relieves the spasm. Stockton recommended epinephrine hypodermically in some instances and reports remarkable relief by the use of this drug. The administration of adrenalin

nucleoprotein, as advised by Rogers, has given relief in a number of instances under our care.

In the intractable forms of pylorospasm which have resisted all medical treatment the operation of pyloroplasty has furnished satisfactory relief.

PNEUMATOSIS

In pneumatosis the stomach is distended with air, expulsion of which is impossible, causing unpleasant expansion of the stomach and dyspnœa. In a large proportion of cases this condition is partly due to a simultaneous cardiospasm and pylorospasm. Relief is at once afforded when the spasm ceases and the air escapes. Pneumatosis is found secondary to certain gastric disturbances, such as atony and dilatation, or is a primary neurosis. It occurs as a continuous or periodic affection, and appears after nervous anxieties or mental strains.

Etiology.—Pneumatosis is found more often in males. In this series it occurred in 8 cases (0.5 per cent.); of these, 6 were males and 2 females.

Symptoms.—Pneumatosis occurs in two forms: In the first it appears in an acute form intermittently with alarming symptoms causing dyspnœa, collapse, rapid and irregular pulse, and cyanosis. The region of the stomach is greatly distended and the patient is unable to relieve himself by eructating. In the second form the attacks come on immediately after meals or some time later, or after some exertion; the symptoms are much like those of the acute form, but may become alarming. The gastric contents are usually normal; occasionally there is a hyperchlorhydria or hypochlorhydria.

Diagnosis.—This is ordinarily made by the features described; all organic conditions must be excluded. It is sometimes mistaken for angina pectoris, but in angina there is no continuous distention of the stomach and expulsion of the gas does not afford relief.

Treatment.—Special attention should be paid to the nervous system. Change of scene, hydrotherapy, and massage often do much to restore the patient to health. Of the medicines used the most important are the bromides, cocaine, or morphine. Boas advises the use of extract of physostigmine, gr. $\frac{1}{6}$ (0.01 gm.), with extract of nux vomica, gr. $\frac{1}{3}$ (0.02 gm.), three times daily. In acute attacks the introduction of the stomach tube will afford instant relief.

PERISTALTIC UNREST (TORMINA VENTRICULI NERVOSA)

Peristaltic unrest is characterized by an excessive and visible peristalsis of the stomach. This condition was first described by Kussmaul as occurring in neurasthenic individuals in whom excessive peristalsis caused annoying sensation and unpleasant contractions of the stomach. In the cases described by Kussmaul the peristaltic movements were visible, as a gastroptosis was present at the same time. Peristaltic movements usually take their origin at the fundus of the stomach and run toward the pylorus; the wave, however, may be antiperistaltic also and run in the opposite direction; occasionally antiperistaltic move-

ments exist alone; cases have also been observed in which peristaltic movements of the intestines were present at the same time.

Etiology.—Peristaltic unrest may occur in one of two conditions: First, due to an obstruction of the pylorus, the stomach exerting itself to overcome the difficulty produced in emptying its contents into the intestines; second, the unrest may occur as a pure neurosis, accompanying neurasthenia or hysteria; as a neurosis it is an exceedingly rare affection, but one case occurring in the series (0.06 per cent.).

Symptoms.—The important symptom is the peristaltic movement of the stomach running from the fundus to the pylorus and at times accompanied by antiperistaltic movements. These movements are usually visible and are felt by the patient. When the stomach is in its normal position the patient may be conscious of the movement, but it cannot be seen. Other symptoms are often present, such as eructations, nausea, anorexia, and the too rapid evacuation of the stomach (hypermotility). General symptoms of neurasthenia are ordinarily present.

Diagnosis.—This is simple if organic obstruction of the pylorus can be excluded, which is usually readily done.

Treatment.—This should be directed mainly toward the neurasthenic condition by change of scene, massage, and hydrotherapy. At times, when the patient is anemic, the best results have followed a well-regulated rest cure. Kussmaul recommended the faradic current. Good results have been obtained by the use of bromides, codeine, and belladonna.

SUBACIDITY OR HYPOCHLORHYDRIA

By subacidity or hypochlorhydria is meant that condition in which the amount of hydrochloric acid and the other constituents of the gastric secretion are lessened. While small quantities of hydrochloric acid are secreted, the quantity is so small that it at once combines with the protein foods. Subacidity is present in certain organic diseases of the stomach, as chronic gastritis and cancer, also during the height of acute febrile diseases. The term *nervous subacidity* can only be applied to those conditions in which all signs of organic disease of the stomach can be excluded. The condition is frequently found with neurasthenia or hysteria, and is present also in certain lesions of the spinal cord, as tabes dorsalis. In this series of 1592 cases, 80 (5 per cent.) represent the number of cases of subacidity or hypochlorhydria; 34 were males and 46 females.

Symptoms. Many cases run their course for a considerable period of time without symptoms; this is especially true as long as the motor function of the stomach is normal, but as soon as this is impaired, fermentation begins in the intestines and distention from gas takes place. The symptoms are not distinctive, and a diagnosis cannot be made until the gastric secretion is examined. As long as the intestinal digestion is normal, symptoms of gastric disturbances are absent and the patient can maintain his normal weight and strength; as soon, however, as the intestinal functions become disordered, diarrhœa sets in and the patient becomes weakened and emaciated. A symptom in 7 cases was burning

with pain about two hours after meals, relieved by alkalis or food and presenting symptoms of acidity.

Diagnosis.—This is arrived at by examination of the gastric contents and finding a diminution of hydrochloric acid. This can however, only be established with certainty by a fractional analysis extending over the entire digestive period. At the same time hysterical or neurasthenic symptoms must be present. By continual observation one is frequently surprised by the various changes this condition undergoes, often to normal acidity or even to hyperacidity. Hemmeter termed it heterochylia.

Treatment.—The diet should consist largely of carbohydrates. Meat should be given in the most digestible form and finely divided; the food should be given in small quantities at frequent intervals. Much attention should be paid to the general health and special treatment given to the nervous system. Hydrochloric acid administered in 10- to 20-drop (1 cc.) doses after meals is useful. Lavage of the stomach is rarely necessary unless the motor function is markedly disturbed and at the same time leads to fermentation. The use of massage and electricity is serviceable in many cases. The saline waters are useful so long as the motor function is normal; as soon as this is disturbed their use should be discontinued.

ANACIDITY OR ACHYLIA GASTRICA

The term achylia gastrica was introduced by Einhorn[1] to indicate a condition in which there is an absence of gastric secretion. The term is simply meant to designate a symptom, the underlying condition being a severe form of chronic gastritis or atrophy of the mucous membrane or some condition wholly neurotic in origin. It is not our province to discuss the cases which are accompanied by a complete atrophy of the gastric mucous membrane, first described in certain cases of pernicious anemia. The use of the term achylia gastrica is best restricted to those cases for which Einhorn first adopted it. In these there is a complete lack of gastric secretion, which persists for many years without ending fatally, and in which the general condition of health frequently improves. The patient often presents no subjective symptoms and can take many forms of food without the slightest discomfort, the small intestine assuming the function of the stomach. In a case of the writer's this condition persisted for twelve years, with gain in weight and but few attacks of intestinal disturbance.

Etiology.—It seems doubtful in most instances whether a complete absence of gastric secretion is due to a neurasthenic condition alone, because, while the neurasthenic condition may improve and disappear, the gastric secretion remains absent permanently. According to many writers it is probable that a more or less pronounced chronic gastritis is present in a large proportion of cases of achylia gastrica. According to Martius, achylia gastrica is produced by two conditions: First, simple achylia gastrica, a primary secretory debility that may be congenital or developed early from hereditary predisposition; and second, atrophy

[1] *New York Med. Rec.*, 1892 **41**, 650.

of the gastric mucosa producing a secondary achylia gastrica. *Simple achylia gastrica* is found in neurasthenic patients, and is associated with inherited weakness of the nervous system and a congenital deficiency in the function of the gastric glands. Hurst calls attention to the primary form of achylia gastrica as an inherited factor in the cases of pernicious anemia occurring in various members of the same family and to those in which members of the family of patients with pernicious anemia are observed to have achlorhydria though apparently enjoying normal health. According to this observer the achlorhydria is not of a specific type but whatever its origin, it predisposes to pernicious anemia. Achylia gastrica may remain latent without making serious inroads upon the general health, especially when the motility of the stomach remains normal and the intestinal functions are undisturbed. There are transitions from the simple forms of achylia gastrica in which these are none or but the slightest changes in the mucous membrane to that form ending in complete gastric atrophy.

According to Stockton, the belief that achylia gastrica may in some instances begin as a simple depression of the functional activity of the secretory glands of the stomach, the result in some cases of neurasthenia, in others as reflex irritation, appears to be gaining rather than losing ground. According to this observer, with the improvement in health gastric secretion is increased, and disappears again with nervous strain. When it is absent for any length of time, it is probable that considerable atrophy of the mucous membrane has appeared, and yet in certain cases Stockton observed the secretion appearing after it had been absent for a year or more. The *secondary forms* of achylia gastrica may be due to various causes, as organic diseases of the stomach, such as carcinoma, syphilis, and chronic gastritis, to gall-bladder infection, sprue, chronic infections, anemia, and not uncommonly arteriosclerosis.

Achylia gastrica is usually found after the thirtieth year of age; it is rarely found in younger persons. It is apparently more frequent in females than in males. In this series the number of cases is 114; of these, 2 represent that form known as atrophy of the stomach, leaving 112 cases (7 per cent.), 57 females and 55 males. As to age, 2 were below twenty, 13 in the third decade, 19 in the fourth, 33 in the fifth, 35 in the sixth, and 10 in the seventh.

Pathology.—There have been so few cases with autopsy that it is not known whether lesions occur in all cases. According to Martius and Lubarsch, and Strauss,[1] a more or less marked gastritis exists in a large proportion of cases of achylia, but there is no means of determining whether the gastritis is the cause or the result of the achylia. Einhorn maintains that there are many cases of achylia in which the mucous membrane of the stomach presents no pathological change whatever, which accounts for the fact that a repair of the condition is sometimes found. Small fragments of the mucous membrane broken off by the stomach tube usually present some degenerative change. The glands show granular degeneration with considerable round-cell infiltration

[1] *Virchow's Archiv*, Bd. **154**.

presenting the picture of a glandular gastritis. It is generally believed that notwithstanding the impossibility of judging the general condition of the mucous membrane from small fragments, in the largest proportion of cases there is some degeneration in the mucous membrane of the stomach. There is no great amount of evidence to indicate that this condition can occur without some anatomical change.

Symptoms.—Einhorn[1] divides achylia gastrica into three groups: (1) In individuals having no gastro-intestinal symptoms and who are in good general health. (2) Patients presenting a greater or less number of gastric symptoms. (3) Patients having apparently no gastric symptoms, but presenting marked intestinal disturbances. The smallest number of cases are in the first group, in which all subjective symptoms are absent. There is no loss of weight, the appetite remains unimpaired, and the diseased condition is usually noted by accident. In this series of 112 cases, only 8 can be counted in this group.

The largest proportion of cases is found in the second group, in which the symptoms are mainly gastric; in this series of 112 cases, 69 belong to this group. The symptoms are loss of appetite, soreness of the tongue, acid or bitter taste, sensations of pain and pressure in the region of the stomach, and occasionally vomiting. The pains are generally mild, often merely a sensation of burning and pressure soon after meals and persisting for some time; in some cases there may be no pain whatever, while in others it may occur with great severity. Nausea and vomiting occur rarely—in but 17 cases of this series. The vomited matter usually contains undigested food particles. Eructations and pyrosis are observed at times; occasionally symptoms are presented similar to those in hyperchlorhydria; that is, the appearance of pain one or two hours after meals, relieved by the ingestion of food. This was noted in 11 cases in this series. Nervous symptoms are also frequently present.

The third group contains those patients without gastric symptoms but presenting intestinal disturbances. In the series of 112 cases these number 35. The most prominent symptom is diarrhœa. The patient complains of little or no disturbance of the stomach, but is affected with symptoms of marked disturbance of the intestines, gurgling in the bowels and intestinal colic. Frequently diarrhœa alternates with constipation. The diarrhœa is probably occasioned by the undigested food mechanically stimulating peristalsis. In addition, a large number of bacteria pass through the stomach and cause decomposition in the bowels. In many instances in the second and third groups, neurasthenic symptoms are frequently manifested, often associated with marked mental depression.

Examination of the gastric contents is of the greatest importance. The following are the characteristics: the amount is very small, only a small quantity of fluid, with bits of unaltered bread; in the morning before the ingestion of food the stomach is entirely empty, with no traces of food from the previous day. The gastric contents are neutral or slightly acid, the total acidity varying between 2 and 6, though occasionally there are instances in which the total acidity is comparatively high. Hydro-

[1] *Diseases of the Stomach*, fifth edition, p. 352.

chloric acid is not present, pepsin and rennin are entirely absent, although the rennet zymogen may still be present; the test for propeptones and peptone reveals negative results, and there is an absence of mucus. A single test following an ordinary Ewald meal is not satisfactory. To establish the diagnosis a fractional analysis should be made during the entire digestive period which must reveal an absence of hydrochloric acid in every specimen obtained. Fragments of mucous membrane often appear in the contents. The motor function of the stomach is usually increased. The pancreatic ferments are ordinarily present in normal amounts.

Diagnosis.—For the most part this is not difficult from the examination of the gastric contents if fractional analyses are made. The most important signs are a constant absence of hydrochloric acid, an almost entire absence of the ferments, and a rather low total acidity. As in nearly all of the cases some alteration has taken place in the gastric mucosa, it is difficult in many instances to distinguish this condition from a chronic gastritis. One must rely mainly upon the presence of nervous symptoms and the complete absence of mucus; a fluctuation in the gastric secretion occasionally indicates the nervous origin. This condition is distinguished from carcinoma by the absence of the typical signs of cancer. The degree of acidity is higher in carcinoma even when free hydrochloric acid is absent; lactic acid is usually present as well as the Oppler-Boas bacillus; the latter is not found in achylia. There is a constant finding of occult blood in carcinoma never observed in achylia; in 50 examinations from 24 cases of achylia in this series, occult blood was never found in the feces. Hemorrhages are never observed in achylia. Roentgen-ray studies of the stomach in carcinoma are valuable in making the diagnosis. When cancer is advanced, no difficulty is presented in making the diagnosis.

Course and Prognosis.—Patients with achylia gastrica may be affected for many years without serious results on their general health. They may even gain flesh when the course is latent for a long period of time. As long as the motor functions of the stomach remain normal and the intestine takes up the functions of the stomach, no serious results are produced; when one or other of the functions are disturbed, the symptoms of achylia manifest themselves and the general nutrition becomes disturbed. Since chronic gastritis is present in most instances, an absolute cure is impossible, even though the symptoms are entirely relieved.

Treatment.—This is mainly dietetic, and although it is necessary to restrict the diet materially, it is most important to insist on the ingestion of sufficient food, as many of these patients have lost weight. The question as to the quantity of food should be carefully considered with an attempt to increase the general nutrition as well as the body weight. In accomplishing this object these facts should be held in mind, namely, to maintain the motor function of the stomach in its normal condition and to prevent any disturbance of the intestinal canal. It is important to arrange the diet so that it can be acted upon easily by the intestinal juices. The food must be broken up into as fine particles as possible and should to a large extent be given in liquid and semiliquid form. Of the liquids, broths, such as barley, rice, or chicken, are to be recommended.

Vegetables are usually well taken; cereals should be eaten after the cellulose has been removed. Peas and beans strained and eaten in purée form are especially useful, since they contain quite a large percentage of protein. Potatoes and rice should be eaten cooked with broth or milk, or as a mush. Eggs are best taken soft boiled. Meats must be given in the most digestible forms, *i. e.*, brains, scraped beef, boiled sweetbreads, and these only in small amount; raw oysters and boiled fish are also permissible. Milk is occasionally imperfectly digested and cream, kefir or koumyss may be substituted. Butter may be eaten on crackers, stale bread, or toast. Tea, coffee, cocoa, and small quantities of wine may be allowed. When symptoms of hyperchlorhydria are manifested, the taking of liquids from one to two hours after meals will afford relief.

Lavage may be used when the gastric motility is impaired. Drugs are not always required; in some cases dilute hydrochloric acid may be given well diluted in 15-drop (1 cc.) doses, three or four times at intervals of fifteen minutes after meals with benefit. For anorexia strychnine combined with the bitter tonics is recommended. When the general nutrition has become very much depressed, excellent results may be obtained by a systemic rest-cure treatment. Whenever possible, outdoor exercise and hydrotherapy are valuable aids in the treatment.

ACORIA

In acoria there is an absence of the sensation of satiety. The patient does not feel that he has eaten enough, no matter whether he partakes of a large or a small meal; the appetite is not increased; it may even be diminished. The cause has not been determined; the theory that acoria is due to an overstimulation of the hunger centre is untenable. The condition may be due to loss of sensation in the stomach.

Etiology.—Acoria occurs as a primary disorder associated with neurasthenia or hysteria, or secondary to other diseases, such as diabetes or disorders of the male sexual organs. Sorrow, shock, or excitement are among the etiological factors. In this series of 1592 cases it occurred in 5 (0.3 per cent.), 3 males and 2 females.

Symptoms.—There is an absence of the sensation of satiation, no matter how large the meal may be. In consequence of the inordinate eating, atony and gastritis may develop. Acoria may be transformed into bulimia. The gastric secretion is usually normal; in this series normal acidity existed in 4 and subacidity in 1; the gastric motility was normal.

Diagnosis.—Acoria must be differentiated from polyphagia and bulimia; in acoria there is an entire absence of the sensation of satiation, while in polyphagia the feeling of satisfaction is delayed to such an extent as to create a constant desire for more food. In bulimia there is an abnormal desire for food, but this desire can be satisfied.

Treatment.—This must be directed toward the cause, which in most instances involves treatment of the general neurasthenia by rest, change of scene, hydrotherapy and massage. Entire relief was effected in 2 cases by a rest cure with psychotherapy. The meals should be carefully

regulated; the patient should be required to eat slowly and masticate thoroughly. Strychnine in ascending doses has been used with some success and arsenic has been found of much value in some instances.

ANOREXIA NERVOSA

Anorexia is characterized by a marked diminution in or the absence of the sensation of hunger, combined with a complete loss of appetite. Anorexia may accompany various organic or functional diseases, or may be a primary neurosis (anorexia nervosa). The loss of appetite may be so great as to cause a most marked disgust or repugnance for food. The cause of nervous anorexia has been attributed to an absence of the tonic contractions of the empty stomach.

Etiology.—Anorexia may be primary or secondary. It is primary as a manifestation of hysteria and neurasthenia; it is secondary to such diseases as cancer of the stomach, chronic gastritis, gastroptosis, acute febrile conditions, chronic nephritis, and other organic diseases. Anorexia nervosa usually begins after some great mental strain, excitement, or anxiety. It is not uncommon in men with sexual disorders (Peyer) and in women with uterine disease, and is often observed in a most aggravated degree in the insane. Opium habitués are commonly affected with this disorder. It is most frequent in females, especially between the ages of fifteen and forty years. In this series of 1592 cases there were 48 cases of nervous anorexia (3 per cent.), 11 being males and 37 females. As to age, 19 were in the second decade, 12 in the third, 10 in the fourth, 4 in the fifth, and 3 in the sixth.

Symptoms.—After some great mental strain or worry a loss of appetite begins to manifest itself; the digestive powers are still normal but the patient shows a lack of desire for food. This lack of appetite becomes more and more decided until the stage of absolute repugnance for food is reached, and the patient loses weight and strength, becomes anemic and pale, the pulse becomes slow and weak, the urine scanty, and marked constipation is evident. With these symptoms, others of a nervous character manifest themselves, and the patient becomes irritable, restless, and sleepless, and, if forced to take food, vomits. If the condition progresses, serious symptoms arise, such as inanition with delirium, slight fever and exhaustion, and the patient may die. When the disease is well marked the patient presents the appearance of tuberculosis; the skin is dry, the abdomen markedly retracted, the eyes sunken, the pupils dilated, and the mucous membranes are pale. Death may be due to exhaustion, pneumonia, or infection.

Diagnosis.—The presence of other nervous manifestations, together with the anorexia and absence of all organic disease, easily leads to a correct diagnosis. In all cases, in arriving at a diagnosis organic diseases accompanied by anorexia must be excluded.

Treatment.—In the milder forms much can be accomplished by insisting that the patient take sufficient nourishment. In order to make this possible the food should be varied and the patient's taste so far as possible be consulted. The bitter tonics at times play an important role; of

these, gentian, colomba, quinine, and strychnine are often useful, especially with dilute hydrochloric acid. Lavage with a bitter infusion, or with a 0.5 per cent. solution of sodium chloride, has been recommended. The nervous system should be built up by means of massage and hydrotherapy. In all serious forms the patient should be isolated in a hospital or sanitarium and placed under a strict rest cure, with forced feeding. The writer feels confident that the lives of a number of his patients were saved by this method of treatment. In those instances in which the patient still refuses to take food, duodenal feeding may be utilized wth marked success. When improving, some form of iron is useful.

SITOPHOBIA

This term was introduced by Einhorn to indicate a special neurosis of the stomach manifested by marked fear of food. He declared that if this condition continued the dyspeptic symptoms gradually increased, even after taking the smallest quantities of food. In consequence the patient loses much flesh, becomes anemic, and develops other symptoms, such as dizziness, headache, lassitude, etc. The fear is due to the unpleasant sensations and pain which may occur after eating, in consequence of which the patient refuses one form of food after another until extremely small quantities of nourishment are taken and inanition results.

Etiology.—Sitophobia may exist secondarily to organic or functional disorders of the gastro-intestinal tract, or as a neurosis. As a secondary condition it is found in ulcer, chronic gastritis, cancer of the stomach, chronic constipation, chronic diarrhœa, gastralgia, and enteralgia. In the series of 1592 cases there were 24 cases (1.5 per cent.), 18 females and 6 males. As to age, 4 were in the second decade, 7 in the third, 3 in the fourth, 6 in the fifth, 3 in the sixth, and 1 in the seventh.

Symptoms.—On account of pain or uncomfortable sensations in the stomach the patient gives up one food after another until he subsists on a very small quantity of liquid food. Severe headaches, nervous manifestations (vertigo, general aches and pains), great loss of strength and flesh, and marked anemia result. Many of these patients consume only from 400 to 1000 calories per day; if this persists, the emaciation continues until the patient finally succumbs.

Treatment.—It is necessary to insist that the patient make every effort to take nourishment, even though it produces pain. In following out this plan he will observe that food which at first occasioned uncomfortable sensations gradually loses this effect and can be taken without distress. At first liquid food alone should be given in the form of milk or egg-albumen, and gradually the diet should be increased to the soft and then to the solid foods. In severe cases marked results are obtained by a well-regulated rest cure. It is an excellent plan to persist with liquid food, such as milk and eggs, for from ten to twelve days, then increasing to very large quantities, and later suddenly placing the patient upon a generous diet without attracting his attention to the same. Occasionally the bromides, belladonna, and hyoscyamus are useful in reducing the sensitiveness of the stomach.

INCONTINENCE OF THE PYLORUS

The pylorus is insufficient when, during digestion, it fails to prevent the chyme from proceeding into the intestines at too rapid a rate.

Etiology.—The condition may be due to an organic disorder, or may exist as a neurosis. The organic conditions that may produce insufficiency are carcinoma or ulcer of the pylorus or chronic gastritis. Boas observed it in duodenal stenosis in which the pylorus was dilated by material accumulating above the stenotic area. As a neurosis, it is very rare. In the series studied there were but 2 cases (0.1 per cent.).

Symptoms.—On inflation of the stomach this organ does not become distended, but gurgling takes place at the pylorus, the escape of air causing increased intestinal tympany. The stomach empties itself too rapidly and there is a reflux of considerable quantities of intestinal contents, bile, and pancreatic secretion into the stomach. This is observed in almost every lavage. Because of the very rapid evacuation of the stomach, diarrhœa is common. The hypermotility can be best observed by roentgen-ray examination.

Treatment.—Because of the passage of the undigested food into the intestines and the diarrhœa, food should be given in a very digestible form. Einhorn recommends direct gastric faradization and occasional lavage. In some instances strychnine has been of service.

ATONY

In atony of the stomach the muscular walls have lost their tonicity, with a resultant motor insufficiency, in consequence of which the stomach is unable to pass its contents into the intestine at the normal rate. Although this condition has long been recognized, great confusion exists concerning its significance. By some authors it is classified as a purely nervous disorder, by others as a form of gastrectasis, while some pass it by in a cursory manner. Kussmaul was among the first to make a distinction between atony and dilatation. He showed that in dilatation due to stenosis of the pylorus or of the duodenum, vomiting is very frequent during the entire course and is a characteristic sign, while in atony it rarely occurs. Boas[1] described this disorder at length as a separate pathological condition, calling it myasthenia (muscle weakness) or muscular insufficiency of the first degree. Stockton points out that gastric atony occurs as a temporary affection, frequently as a sympathetic reaction to toxic, reflex and general nervous disturbances.

Bettmann emphasizes the fact, that muscular insufficiency is by no means implied in the term atony as it is now employed and that atony may exist without producing delay in the emptying-time of the stomach. He points to Cannon's investigations in which it was shown, that when an organ with walls of smooth muscle is flaccid and toneless, distention occasions no response and that only when the muscles are shortened and resilient does stretching result in contraction. Tonicity is a fundamental

[1] *Specielle Diagnostik und Therapie der Magenkrankh.*, vol. 6, Auflage, S. 518.

necessity for the appearance of rhythmic movements in the stomach and depends for its development and maintenance upon the normal activity of the vagi nerves. The sympathetic nerves (splanchnics) as opposed to the vagi nerves have a marked inhibitory effect on the gastric muscles.

Barclay maintains that the ability of the stomach to contract well upon its contents and to retain its tubular form is the expression of gastric tonus; atony, he defines as the failure of the gastric muscle to maintain the tubular form of the gastric wall against the action of gravity. According to this view, in many instances of atony peristalsis may be normal. Gastric tonus depends to a marked degree upon the central nervous system, fright often producing an atonic state.

Etiology.—As regards causation, atony may be primary or secondary. Primary atony is found in persons who have been in the habit of consuming large quantities of indigestible food; the excessive use of fluids especially predisposes to this disorder; frequently, however, no such cause is assignable. Atony may be secondary to many other diseases, such as those of the brain and cord, anemia, tuberculosis, and diseases of the gastro-intestinal tract, such as gastroptosis, enteroptosis, constipation, chronic gastritis, and nervous dyspepsia. Cholelithiasis is not an infrequent cause. According to Peyer, it is often found as a neurosis secondary to disease of the generative organs in males. Bamberger finds it frequently congenital, and according to Zweifel it is not uncommon in children, due in many cases to improper feeding. Pfungen has shown that atony often originates during the period of puberty. It is not improbable that the precocious appetite at this age, leading to the consumption of much indigestible food, is the cause. No age seems to be exempt and it appears with equal frequency in males and females.

Symptoms.—Most patients complain of a loss of appetite, although in rare instances the appetite may be fully maintained, at least in the first stages. When the condition is secondary to nervous disorders the appetite may even be increased (Peyer). A feeling of pressure or fulness comes on, usually during or after meals, and this is especially marked after the ingestion of fluids. In light forms the distress reaches its height immediately after meals, and gradually passes off during the next hour, to be again aggravated by the smallest amount of food. In severer forms it may be so great as to continue with intensity for hours after meals, and become still more aggravated when food is taken again. This feeling of pressure is accompanied by heart-burn, pyrosis, and eructations of gas, but rarely by vomiting. The quality as well as the quantity of food ingested is productive of this symptom; fluids are most likely to induce pressure. Constipation is almost constant and a dull headache is often present and at times vertigo. Nervous symptoms of various kinds may be present and the disorder is frequently mistaken for neurasthenia.

The stomach is found to be enlarged, so that the greater curvature reaches to or below the level of the umbilicus. Peristaltic and antiperistaltic movements of the walls of the stomach may occasionally be visible. With but small quantities of fluid (from 250 to 300 cc.) in the stomach, splashing sounds may be readily produced. In atony the stomach is not only enlarged but its motor function is also markedly impaired. An

important test is the condition of the fasting stomach which should be empty and free from all food remains. In cases of dilatation greater or smaller quantities of food will be found. Boas devised a test of great service. His test supper consists of white bread with butter, cold meat, and two cups of tea taken at 8 P.M. In atonic conditions the stomach will be empty the next morning, but in dilatation it still contains food remains.

Examination of the *gastric contents* is of great importance. The expression one hour after an Ewald test breakfast shows large quantities of solid contents, not separating into the characteristic three-layered fluid of gastrectasis and not containing yeast spores or sarcinæ. The contents show in most cases a normal proportion of hydrochloric acid, pepsin, and casein ferment. According to Boas, at the very beginning of atony of the stomach, through constant mechanical irritation of food, an increased acid production results; in fact, hypersecretion may be produced. In other cases there may be a condition of subacidity.

Among frequent complications may be mentioned gastroptosis, enteroptosis, and dropping of the right kidney. Atony of the intestine is not an infrequent concomitant of atony of the stomach; indeed, both may be present for years, and it may be difficult to tell which is primary. Gastric vertigo probably depends in most cases upon atony (Boas).

Diagnosis.—Atony must be differentiated from nervous dyspepsia and dilatation. According to Bamberger[1] the variability and rapid change of symptoms, the presence of other nervous symptoms, the normal and increased appetite, and the absence and rapid disappearance of the gastric disturbance, distinguish nervous dyspepsia from atony. At times a diagnosis is difficult and sometimes impossible. It must not be forgotten that atony is frequently a complication of nervous disorders.

From dilatation, atony is diagnosed by the absence of food remains in the fasting stomach, by the absence of the three-layered fluid of dilatation and by the absence of sarcinæ and yeast. There is a marked diminution in the secretion of urine in dilatation but not in atony.

Prognosis.—Atony of the stomach is a chronic disorder and may last for years. It is quite amenable to treatment, and, although it may not be perfectly cured, the patient may be relieved of all suffering. It may pass into gastrectasia years after, but this is rather rare.

Treatment.—Since atony is frequently caused by injudicious and too rapid eating, people with feeble digestive powers should exercise special caution to eat slowly, masticate thoroughly, and avoid indigestible food. Persons with atony of the stomach should eat small quantities of food at frequent intervals. Since water is not absorbed in the stomach to any extent, it is advisable that the quantity of fluids taken should not exceed 1½ liters a day; this amount should include all fluids. If the thirst is very great, fluid may be given by the bowel.

The use of milk in large quantities has been recommended, but is not to be advised when the patient is able to go about, since the weight of large quantities of milk may overdistend the stomach; when a rest cure

[1] *Krankh. der Chylopoet. Systems, Virchow's Handbuch*, 1855, Bd. **7**, I, 270.

is instituted, milk is often well borne, even in large quantities. The diet in atony varies according to the nature of the gastric secretion. In superacidity a liberal meat diet, consisting especially of chicken, beef, and mutton, is recommended; fish, eggs, hard and soft boiled, are also permissible; the vegetables should be selected with care; carrots, peas, and cauliflower may be given, but must be mashed and strained. Potatoes, rice, and grits are also allowed. Butter is the best form of fat.

Alcohol is, as a rule, not well borne, and its use should be prohibited. In cases in which there is an absence or a diminution of acid in the gastric secretion the lighter forms of meat, such as the white meat of chicken or fish, sweetbreads, stewed chicken, or raw scraped beef, should be allowed; vegetables, on the other hand, must be given in somewhat larger quantities. The treatment of chronic constipation requires special mention and the main reliance must be placed on the diet. Such food should be given as excites intestinal peristalsis, Graham bread, vegetables, such as carrots, beans, tomatoes, peas, turnips, macaroni, stewed and raw fruits, buttermilk, honey, and cider. This form of diet will often overcome the constipation without the aid of drugs. When this proves ineffectual, enemata of various kinds, especially of oil, may prove beneficial.

In atony lavage is quite superfluous, and is not recommended. Of great value is massage of the abdomen, the effect of which is to increase the peristalsis of the intestine and to strengthen the abdominal walls. In regard to medicinal treatment, preparations of strychnine seem to serve the best purpose; strychnine sulphate or the extract of nux vomica may be given in pill form. To allay the feeling of pressure, a constant and annoying symptom, the extract of belladonna is prescribed. When there is a diminished secretion of hydrochloric acid, 15-drop doses of dilute hydrochloric acid, several times after meals, are indicated. With increased acidity, sodium bicarbonate should be ordered after meals.

POLYSYMPTOMATIC NEUROSES. NERVOUS DYSPEPSIA OR NEURASTHENIA GASTRICA

The polysymptomatic neuroses are characterized by an unusual multiplicity of symptoms, in contradistinction to the monosymptomatic forms, in which one symptom is prominent or alone observed. The most important and typical example of a polysymptomatic neurosis is nervous dyspepsia, in which the symptoms are manifold and yet no organic changes can be detected. According to Leube's original conception, the term nervous dyspepsia was intended to cover that group of cases in which the secretory and motor functions of the stomach were normal while the patient was suffering from manifold subjective symptoms. Later Leube included in this class a group of cases manifesting changes in the gastric secretion and motility.

There are two forms of nervous dyspepsia: (1) That group in which no anatomical changes can be detected in the stomach. (2) That group in which the nerves supplying the stomach are involved in anatomical changes, with consequent changes in the gastric secretion. Boas described a third form originating "reflexly from disturbances in other organs, such

as the kidneys, generative organs, and particularly the intestines." In addition constitutional diseases, such as diabetes, tuberculosis, and syphilis may form a basis for the production of this condition. Nervous dyspepsia is also characterized by the fact that all the functions of the stomach, motor, secretory, and sensory may be disturbed at the same time. Nervous dyspepsia, accompanying organic diseases of the stomach, can be so combined with it that most careful study may be necessary to differentiate between the primary and secondary affection.

Etiology.—As nervous dyspepsia is frequently associated with general neurasthenia, all conditions bearing an etiological relationship to neurasthenia are causative in the production of this disorder. A large number are due to worry, anxiety, reverses, overwork, sexual and alcoholic excesses, and also to the abuse of tea, coffee, and tobacco. Certain cases come from diseases of the blood, constitutional diseases or such diseases as tuberculosis and diabetes; other cases occur reflexly, the primary cause being eye-strain, genito-urinary disturbances, mental disturbances or the puerperal state. In this series of 1952 cases there are 268 (16.5 per cent.) cases of nervous dyspepsia, 154 males and 114 females. As to age, 33 were in the second decade, 55 in the third, 55 in the fourth, 68 in the fifth, 38 in the sixth, and 19 in the seventh. It occurs more frequently in males than in females.

Pathology.—In 41 patients with nervous dyspepsia Jurgens[1] found a degeneration of Meissner's and Auerbach's plexuses after death; so that in a certain number of cases there appears to be an anatomical basis.

Symptoms.—It is characterized by the multiplicity of its symptoms, varying greatly in intensity, mode of onset, and frequency. The most prominent is the gastric discomfort after meals, although the distress is not dependent upon the quality and quantity of food ingested, but rather upon mental strain, worry, or excitement. It often happens that the most digestible food causes distress, while the most indigestible food is borne without discomfort. The gastric distress is characterized by pressure, fulness, eructations, distention, flatulency, peculiar sensations in the stomach, and heartburn. One food after another is discarded on account of the discomfort produced until sitophobia results with marked inanition. Manifestations of neurasthenia are often present, headache, depression, vertigo, palpitation of the heart, lassitude, loss of strength, globus hystericus, and insomnia. The appetite is usually capricious, developing into a bulimia, and followed quite suddenly by complete anorexia. The general condition is not usually affected, although in some instances the emaciation may be so extreme as to suggest serious organic disease. The periods of well-being alternating with those of discomfort are rather characteristic as also the variations in the intensity of the symptoms from day to day. The abdomen is usually sunken, occasionally distended with gas, accumulating often in the region of the cecum and in the colon at the splenic flexure; the abdomen is often tender at the distended areas, but the pain is relieved by the expulsion of the gas. The bowels are, as a rule, constipated.

In the larger proportion of cases the *gastric secretion* is normal; occa-

[1] *Verhand. des III Congresses f. Medicin*, S. 253.

sionally there is subacidity and less often hyperacidity. A characteristic feature is the fact that when anacidity exists the ferments are not generally diminished in quantity; not infrequently marked variations in the secretions are met with (heterochylia). In this series the gastric analysis showed normal acidity in 163, subacidity in 57, hyperacidity in 35, and heterochylia in 13. As a rule, the motor function remains normal, although occasionally an atonic state of the stomach may occur. In the 268 cases slight atony existed in 57; gastroptosis is not infrequent and occurred in 41 of this series.

Diagnosis.—This is made by the absence of all indications of organic disease, together with the general nervous symptoms, associated with the digestive disturbances. It is further strengthened when the motor and secretory functions of the stomach are found normal. Greater difficulty is manifested when these functions are not perfectly normal, but even then the symptoms are so far out of proportion to the changes that these slight variations will not account for the condition found. The discomfort is not dependent upon the quantity and quality of food; indigestible food does not increase the distress.

It is always necessary to exclude all organic conditions but this is not always a simple matter. Boas advises the following plan in doubtful cases: A very easily digestible diet is given the patient, similar to that ordered during the third week of an ulcer treatment; while on this diet, the subjective symptoms are observed for three to four days, when other foods are gradually added, such as sauces, vegetables, desserts, and various fruits. The symptoms are now compared with those during the first period. In nervous conditions they do not increase on the fuller diet but often lessen, while in organic disease they increase.

Nervous dyspepsia is distinguished from *chronic gastritis* in that the gastric disturbance is more or less directly dependent upon the quality and quantity of food ingested in the latter condition, while the gastric contents contain large amounts of mucus not observed in nervous dyspepsia. There may be an absence of free hydrochloric acid in both disorders, but an absence of enzymes is not usual in nervous dyspepsia. It is differentiated from *ulcer* by the absence of a localized, painful area in the epigastrium which, although it may be present for a few days at a time, is not constant; by the absence of hematemesis and occult blood in the stools and by the sudden disappearance of all discomfort. Often the diagnosis can only be made after observing the effect of an ulcer cure.

In certain instances of nervous dyspepsia the emaciation is so intense as to suggest *carcinoma*, especially if there is an absence of free hydrochloric acid. A correct diagnosis is arrived at by noting the age, the duration of the disorder, and determining the presence or absence of motor insufficiency as well as of occult blood in the feces.

Prognosis.—This is not always favorable, although, as a rule, it is not a fatal disease. It may be obstinate and resist all treatment; the milder forms usually yield readily to proper treatment, while the severer ones continue over a long period before entire relief is afforded. There may be a rapid loss of flesh and strength and finally death. Relapses are not uncommon.

Treatment.—Boas stated that "in the larger proportion of cases of nervous dyspepsia drugs are not indicated. The patient should be taught that recovery cannot be brought about by the use of drugs, but only by a sensible mode of living and following the laws of hygiene." In all cases in which it is possible to determine the cause, this should be overcome, *i. e.*, all intestinal disturbances should be corrected, anxieties and worries relieved, and sexual disorders treated. When no cause can be determined, the treatment should be directed to the general neurasthenia. This is often best combated by change of scene. The diet should not be too restricted, but nourishing food, without any attempt at a too rigorous diet, should be prescribed. In those cases in which milk is well tolerated it may be given in large quantities; when it is not well borne, buttermilk, kefir, or koumyss may be substituted. The patient's appetite is humored, and he may be allowed to eat any food he can digest. Alcohol is prohibited, or given only in very small quantities. In severe cases a well-conducted rest cure produces the best results. In those instances in which the patient has lost much flesh and strength, the most beneficial results are obtained by means of forced feeding and isolation. Hydrotherapy and massage are useful. Rosenheim recommended the gastric douche, while others practice lavage. Of the medicinal remedies used the milder preparations of iron, arsenic, bromides, and the preparations of valerian must be noted.

CHAPTER IX

ORGANIC DISEASES OF THE STOMACH

By CHARLES F. MARTIN, M.D.

AND

COLIN SUTHERLAND, M.D.

GASTRIC ULCER

Synonyms.—Peptic ulcer; simple ulcer of the stomach; round ulcer; perforating ulcer; ulcus ventriculi (Frank); Cruveilhier's disease (Cruveilhier was the first to give a good clinical and anatomical description of the condition). The first name is doubtless the best, for these ulcers are not always round, neither are they always chronic, nor do they always perforate, but they occur wherever gastric juice flows. Erosions of the gastric mucosa are probably often early conditions of gastric ulcer, both as regards etiology and morbid anatomy, and the subsequent autodigestion affords the more typical appearance of the simple ulcer. Hemorrhagic erosion, while not really an ulcer, may and does readily lead to it.

Definition.—A more or less progressive destruction, beginning in the mucosa and sometimes extending to and even through the deeper layers of the stomach wall, of the nature of a degeneration or a necrosis. These ulcers occur practically only where the gastric juice flows, and are found, therefore, only at the extreme lower end of the œsophagus, in the stomach itself, and in the portion of the duodenum above the opening of the common bile duct. Such ulcers may be acute or chronic, with or without tendency to cicatrization and healing. They leave an open loss of substance, usually round or oval in shape, with edges which are, as a rule, clean cut in the acute and subacute cases, more irregular in the chronic. Acute exacerbations of chronic ulcers are commonly mistaken for acute ulcers, and the subsidence of the acute period is often mistaken for the cure.

Statistical.—Statistics in regard to gastric ulcer are, on the whole, of very doubtful value. Advances in our knowledge of diagnostic methods including radiology and the greatly increased experience from laparotomies, have materially altered our views of the incidence, the site, the origin and the nature of gastric ulcer. The unsatisfactory grouping of cases of peptic ulcer with reference to etiology renders statistics still more unreliable. Ulcers occurs in about 1 per cent. of hospital admissions, while 44 per cent. of autopsies reveal this lesion. As a cause of death, ulcer occurs in 0.1 per cent. of cases. There is a marked increase in the number of hospital admissions, *e. g.*, in the London Hospital during the decade up to 1908, 136 cases entered, of which 54 were males. In the next decade to 1919, 235 admissions were recorded, 141 being males. The Mayos state that only 25 per cent. of peptic ulcers occur in the stom-

ach, the majority being duodenal, and of these, 75 per cent. occur in men. Hemorrhagic erosions, however, are much commoner than is generally believed and arise almost invariably from infection. It is the acute ulcers which are more common in women, and in such cases hemorrhages are much more frequent.

Geographical Distribution.—The regional differences are great, the most marked being, as Rutimeyer has shown, between North America on the one hand (0.12 to 1.28 per cent.) and Central Europe on the other, (0.54 to 3 per cent.) clinically. Their pathological variations are even more marked (0.85 to 2.35 per cent. as against 1.30 to 11.0 per cent.). For the reasons already cited it does not seem possible to obtain useful statistics on regional differences in distribution.

Etiology and Pathogenesis.—The causes which induce peptic ulcer are many. The main etiological factors concerned are:

1. A local circulatory disturbance, perhaps an imported infectious agent (germ or toxin).
2. An injury to the mucosa.
3. The presence of the gastric juice, with its acid and its enzyme. Peptic ulcer occurs only where the gastric juice flows.

The combination of these three factors seems to permit of autodigestion. It appears to be well established that an essential feature is a local disturbance of the circulation (embolic, thrombotic, arteriosclerotic, vasomotor, etc.). The supply of nutrition to the mucosa is thereby affected, and there is lessened resistance within the focal area, and the gastric juice more readily digests it. If the gastric juice be hyperacid, the necrosis is less liable to heal. Hauser, Ophüls and others emphasize the importance of arterial conditions as factors in the etiology.

Much stress has of late been laid upon infections as a cause of ulcer, and many observations have been made to substantiate this theory. Smithies finds 33.7 per cent. and some other statistics corroborate this. Focal infections, more particularly in the mouth (tonsils and teeth), in the appendix and gall-bladder have repeatedly been noted, and experimental evidence has been held to prove this assertion. Rosenow and others regard certain strains of streptococci as more or less specific for gastric ulcer, and claim to have induced ulcers in dogs and rabbits by injection of cocci grown from other gastric ulcers, as well as from the tonsils, teeth, appendix and gall-bladder.

With reference to the appendix as an etiological factor, Braithwaite found that the flow of lymph from the ileo-cecal angle is frequently diverted to the region about the pylorus and duodenum, and when this aberrant lymph is infected, ulcers may readily arise.

Many years ago, Letulle, Martin and others called attention to the coexistence of ulcer with various infective diseases, as also to the fact that the gastric mucous membrane was a favorable site for infective processes. It may be, however, that these infections are accessory to rather than direct etiological factors.

R. T. Morris mentions as salient features: (1) Terminal arteries; (2) elective affinities for toxins; (3) desensitization, and (4) perhaps some endocrine dysfunction and wrong hormone production.

The toxins induce either endarteritis or a spasm and closure of the lumen of the vessel, with anemia, and, later on, necrosis. In this way, the area is vulnerable to attacks of ferments, microbes or antibodies.

The *oïdium albicans* has been mentioned as one of the principal causes for chronicity of gastric ulcers, as well as of perforation. The relations of *spirochetes* to gastric ulcer will be dealt with elsewhere.

It should be remembered that experimental ulcers produced in dogs and cats are not necessarily applicable to humans; in many of these lower animals, ulcers are already so frequently present that Kawamura has somewhat deprecated the significance of these observations.

Age.—Gastric ulcer is less common between fifteen and twenty-five years of age, than was previously supposed (21 in 1933 cases (Choyce)), though the age incidence differs according to the sex. In infancy it is rare, no case occurring under ten years in 262 autopsies on cases of ulcer at the Berlin Pathological Institute. Cutler, Rehn, Martha Wollstein and others have recorded quite a number of instances in infancy and childhood, though many experienced pediatrists have never observed a case clinically. Probably in the young, metabolic and infective factors play an important part, and healing is easier. The symptoms seem less distinctive than in adults, and depend chiefly on evidences of blood in the vomitus or feces, for which many other causes than ulcer may be found, *e. g.*, hemorrhages from the nose, throat, lungs, or from the mother's breast; or, again, from general constitutional diseases, such as scurvy, purpura, the malignant exanthemata, cirrhosis of the liver, etc. Perforation seems to be relatively more common in children than in adults. Henoch found ulcers occasionally in the newborn, and, according to Osler, they are sometimes found in the fetus. An example of the presence of ulcer at the other extreme of life is reported by Eleanor C. Jones in a man, aged eighty-four years, with a past history of gastric ulcer thirty years before, and in whom, at death, a fresh ulcer was found next to the scar of the old healed ulcer. Surgical observations have demonstrated a much greater frequency of ulcer in the later decades of life than was formerly believed. Arterial factors doubtless obtain at this period of life and such ulcers are usually much more chronic.

Riegel's statistical table (compiled from clinical cases) is interesting:

	Riegel's table.			The writer's combined clinical statistics.	
Age.	Men.	Women.	Total.		
0 to 10 years	..	..	..	1	0.14 per cent.
10 to 20 years	8	35	43	85	12.00 per cent.
20 to 30 years	29	62	91	259	37.00 per cent.
30 to 40 years	35	22	57	186	26.50 per cent.
40 to 50 years	36	11	47	110	14.00 per cent.
Over 50 years	18	4	22	63	9.00 per cent.
Total	126	134	260	704	

Sex.—Statistics on this point vary greatly and one should not attach too much importance to individual reports. Clinically, recent statistics show a preponderance of males, according to Mayo, 75 per cent. are in men, though acute ulcers are commoner in women, of 87 acute perforated

ulcers 47 were in females. Duodenal ulcer seems more common in males, according to most writers; R. T. Wilson's statistics are important because of the large number of cases observed and confirmed by roentgen-ray and by operation. They show that of 363 cases, 126 were gastric (38 in females and 88 in males) and 237 were duodenal (65 in females and 172 in males).

Occupation.—This bears some relation to ulcer only in so far as injury to the mucosa or the circulation may occur, and no walk of life appears to be exempt. According to some authorities, cooks are predisposed, presumably because of their habit of swallowing foods which irritate the mucous membrane. In Payne's statistics only 3 out of 50 females were cooks. Workers in metals (Bouvert), glass and porcelain factories (Bernitz), who are in the habit of swallowing dust particles, are thought by some to be more liable; so also tailors and shoemakers because of their posture and occupation leading to abdominal pressure; but in all these there would seem necessary some preliminary injury to the mucosa or the circulation.

Dietetic Errors.—In themselves these are scarcely to be regarded as the cause of true gastric ulcers except when they create *trauma*. Where a combination of circumstances may induce hyperacidity, disease of the mucosa, or other conditions, to *assist* formation of gastric ulcer, it may be that indigestible foods or dietetic indiscretions aid the development of the condition, or may be, at least, regarded as antecedents.

Trauma.—As a cause of gastric ulcer this may be external or internal. Internal trauma, arising from hot foods, corrosives, foreign bodies, and mechanical and chemical irritants, may be predisposing factors. External injury, as from a blow or, perhaps, even from mere compression, may cause ulcer. One must not confuse the production of mere gastric hemorrhage after external injury with ulcer. Mattison gives 1.5 per cent. of ulcers as due to trauma, and Smithies' statistics are approximately the same in 522 cases. The symptoms and signs followed almost immediately. In 17 out of 25 cases there was no previous history of ulcer. The prognosis of these cases does not materially differ from those of other forms.

Ritter produced experimental submucous hemorrhage in dogs after inflicting blows on the stomach, in one case causing even a separation of the mucous membrane, and it was his opinion that injuries predisposed to ulcers through the subsequent action of the gastric juice. He describes an incident in which injury in the epigastric region was followed in eight days by hematemesis and other signs of gastric ulcer. Fertig describes an apparently undoubted case in which as a result of a kick in the abdomen, four gastric ulcers were found at autopsy. One may conclude, however, that such injuries sometimes provide the original lesion for the later formation of true ulcer. The same probably holds true of the theory of Rokitansky and Rindfleisch and Key, that ulcers arise from hemorrhage and subsequent erosion.

This seems to be the view taken by Richardière, whose traumatic ulcer cases are classed in two groups, the one, acute cases healing rapidly, the other cases running a course similar to ordinary chronic ulcer. The difference in the result may depend on the condition of the gastric juice,

especially as regards its acidity. Violent emesis as a mechanical factor in the causation of gastric ulcer is a doubtful cause and much more likely to be associated with some underlying condition, such as uremia.

Previous gastric trouble as an etiological factor is of doubtful importance, except when hyperacidity and hypersecretion have existed. It is difficult to draw the line between the symptoms of previous gastric disturbances and the early signs of ulcer, for a supposed preliminary gastritis may have been the indefinite symptoms due to an already existing ulcer. C. H. Miller believes that inflammatory swelling and rupture of lymphoid follicles may induce erosions which may develop later into true ulcers. Gastric ulcer is essentially a *necrosis*. It is doubtless due primarily to a circulatory disturbance, be it arterial, venous, or capillary, and when once a defect occurs it is prevented from healing by the action of the gastric juice. Excessive acidity makes the ulcer chronic. This tendency to chronicity with lack of healing power is the distinguishing characteristic of simple ulcer as opposed to a mere traumatic erosion.

Relation of Circulatory Disturbance to Gastric Ulcer.—Various circulatory disturbances may account for the early changes which produce lesions. Heart disease though frequently associated with gastric ulcer has only an indirect etiological connection. Chlorosis and anemia are thought by many to be predisposing factors, while, *vice versa*, chronic ulcer certainly often leads to anemia. Samuel and W. S. Fenwick hold that a definite relation exists between ulcer and anemia, and 72 per cent. of their cases showed symptoms of anemia before serious ulcer symptoms developed. There is little doubt that when anemia coëxists with acute or subacute ulcers, the treatment of the blood conditions materially aids the ulcer cure. Perhaps, as Cabot and Stengel suggest, the anemia is often due to hemorrhages, though in Fenwick's case it occurred without these. There can be little doubt that ulcer occurs more commonly among those who are anemic than in persons in perfect health.

Arteries.—*Embolism.*—Virchow, Orth and Payr insisted on the embolic nature of the disease. Payr's experiments established the etiological relationship of ulcer with disturbance of the circulation. The fact that the arteries are not terminal implies that ulcer is not the necessary invariable result, and often, too, where ulcer exists, no emboli can be found. The same holds true with thrombosis. Arteriosclerosis comes under the same head (Howard), as, too, would ligature of the afferent vessels (Litthauer). Minute infective emboli as a factor have been considered.

Vascular Spasm.—Contractions of the muscularis mucosa, including the afferent vessels (Talma, Lichtenfeld, Bergmann, Rossle) have been associated with gastric ulcer. It is doubtful, however, if contraction of the muscularis mucosa would affect the arterial rather than the venous portal system. Arterial spasm, however, may be accountable for the acute perforating ulcer.

Venous.—Hemorrhagic infarction and submucosal hemorrhages from external trauma (Ritter, Fertig, Kronlein), and internal, through chemicals and irritating substances, affect the surface of the projecting folds of the mucous membrane. Aschoff has insisted on the importance of this factor. Whatever the circulatory disturbance may happen to

be—and any one of these may institute an early lesion—other factors must be superadded to produce the ordinary ulcer, for without them healing will occur. *The mechanical factor* is of great importance and helps to account for the production of some forms of circulatory disturbances. Aschoff has drawn attention to the early origin of ulcer on the top of folds of the mucous membrane, especially at the lesser curvatures, where two large rugæ exist, exposed to attrition, to contact with thermic, chemical and mechanical causes of injury, as well as to the effects of muscular spasm. There would seem to be certain points in the cavity of the stomach where contact with irritative substances is more constant and where food is retained for a longer period, thus keeping up the irritation. It is at these points that ulcer is most frequent.

Nervous influences originating in the central nervous system, in the cœliac ganglia, in the splanchnic, the vagus, and elsewhere, play a part which is only subordinate. It is possible that they produce the circulatory disturbance which, later on, develops into an ulcer. Eppinger and Hess suggest that the equilibrium between the vagus and sympathetic systems is sometimes disturbed, resulting in spasm of the muscularis mucosa, which helps to produce circulatory disturbance and ulcer. Van Yzeren, and later, Ophüls, induced ulcer in rabbits by means of bilateral resection of the vagi below the diaphragm. The explanation is not clear. There may be a spasm of the arterioles or of the smooth muscle of the gastric wall, causing anemia, or some destructive process. It has been held that muscular spasm may be associated with the development of ulcer, and this occurs in appendicitis, in renal calculi, and other such internal causes. Rossle calls gastric ulcer the "secondary disease" and noted its association with such conditions above mentioned. G. von Bergmann attempted to show that in cases of gastric ulcer there are already various stigmata to show this want of harmony, *e. g.*, hypersecretion, spastic contractility of the muscles, spastic constipation, cold extremities, and other evidences of the so-called neuroses.

Lack of Antibodies.—According to Wienland and MacCallum, ulcer is due to the lack of "antipepsin," an antibody normally formed by gastric epithelium. There is either failure to produce it or it is destroyed by the hyperacid juice. In this way immunity from autodigestion is gone.

Hyperacidity and Hypersecretion in Gastric Ulcer.—Physiological and clinical observations have appreciably altered our knowledge and conception of the significance of the secretion of gastric juice. Normally the acidity of the stomach is now known to be about 0.4 to 0.5 per cent. instead of 0.2 per cent. This higher titre does not represent a hyperacidity, however, and Carlson insists that the acidity of the juice increases only with the rate of secretion. The amount of normal secretion during twenty-four hours has not been accurately estimated. There may be 1500 cc. or double that amount. Essential hypersecretion, as described by Reichmann, does not exist. Gastric juice can produce anatomical or functional disorders only when it acts upon tissues or mechanisms that are already pathological; and, on the other hand, no known disease produces hyperacidity. It would seem, then, that the importance of the gastric juice has been much magnified, and that the motility of the stomach is of much more importance than the secretion.

Gastric ulcer increases no doubt the tendency to *spasm*, usually at the site of the ulcer, either by irritation of the organic tissues or reflexly. There is thus more peristalsis, with spastic contraction, at the pylorus, and delay occurs through the functional obstruction. It is likewise recognized that when, under certain conditions, spasmodic closure of the pylorus occurs, any hyperacidity that exists is chiefly associated with a prolonged stay of food in the stomach which calls for a further response on the part of the gastric juice, and therefore hypersecretion.

In gastric ulcer, great variations occur in the amount of secretion. One may get, and usually does get, an increase in the secretion of hydrochloric acid, though, on the other hand, normal figures may obtain, or there may be complete achylia. Carlson regards as pathological such figures only as indicate a diminution of secretion. The variation in the gastric juice may be accounted for by many factors, but there is no evidence that an ulcer *per se* alters the activity of the gastric glands. Among the causes for these variations may be cited the following:

1. Different *stages* of ulcer formation, often according to the anatomical changes that have occurred.

2. Different *periods* in the stage of ulcer development.

3. Different *sites* of the ulcer, *e. g.*, pyloric ulcers with stenosis almost invariably show an increased secretion with retention of food. Schryner and Singer believe that this hypersecretion occurs chiefly with pyloric and duodenal ulcers, while it varies greatly when ulcers occur in the body of the stomach.

4. The degree of *motility*. Hypermotility, from irritation of the muscle beneath, often causes hypersecretion, and this may be entirely reflex unless an obstruction is present. The work of Alvarez has been most illuminating. Normal peristalsis proceeds from the cardia to the pylorus; at the cardia there is much greater tone but less amplitude of the peristaltic wave; while, on the other hand, at the pylorus there is less tone but greater amplitude. Under normal conditions, a wave starting from the cardia travels faster along the greater curvature to reach the pylorus at the same time as that on the lesser curvature. When ulcer occurs on the lesser curvature, Alvarez found that the rate of progression of peristaltic waves is altered, one wave reaches the pylorus before the other, *i. e.*, a block is caused, and so we have stasis, even when the pylorus is patulous. Hypersecretion is a natural result.

5. The degree of *neutralizing power* may be another factor in determining the amount of secretion found.

6. The degree of *pain*. Hardt, in studying the cause of pain by means of stimulants, kymographic observations, and acidity production, showed a definite relation between pain, the variations in acidity and peristalsis. It appears that the quiescent period was synchronous with lessened contraction, lessened tonicity and lessened inflammation, and correspondingly less acid secretion. Logical therapy in such cases would thus be to reduce peristalsis by whatever means possible.

7. *Metabolic disturbances* are considered by Molner and Osaki as a factor. Hypersecretion, they believe, is often a part of a general metabolic disturbance of the sodium-chloride excretion.

8. Hemorrhages are often followed by increased acidity.

9. *Undernutrition* as a cause of hypoacidity has been observed.

Hyperacidity is associated with stasis in the stomach, due in part to increased activity of the pyloric sphincter and in part to the increased secretion of gastric juice, but, as has been said, this is a hypersecretion rather than a high acid titre. In general, about 50 per cent. of ulcers show hypersecretion but it is generally recognized to-day that such hypersecretion is due to a reflex after the ulcer is formed, *i. e.*, it does not antedate the ulcer. Of one thing we may be certain: neither hyperacidity nor hypersecretion is necessary to the diagnosis of ulcer for the amount of secretion is less important than the history and the symptoms, especially if they be of long duration.

The examination of the fasting stomach, as emphasized by the French School, is evidently of considerable importance; nevertheless, repeated observations show that even in the empty stomach, the amount of free hydrochloric acid may vary within very wide normal limits (0.08 to 0.04 per cent.). It would seem, then, that continuous secretion is, after all, a normal process. From the therapeutical standpoint, the action of foods upon the secretion is of considerable importance. Meats induce higher secretion, while fatty foods do so, if at all, only after a long latent period (fifteen to thirty minutes). Pure carbohydrates induce apparently little or no secretion, and the same may be said of fats. Sodium chloride definitely stimulates secretion (Bickel). Sodium bicarbonate, however, depresses secretion according to most authorities, though others believe that it stimulates production of acid. There seems no doubt that the giving of large doses of sodium bicarbonate promotes instant relief in cases in which the symptoms of acidity are present.

Pathology.—Situation.—About 80 to 90 per cent. of all gastric ulcers occur at or close to the pylorus, more commonly on the posterior surface and the lesser curvature. Over 30 per cent. occur in the lesser curvature alone; over 40 per cent. in the pylorus alone, and 70 to 90 per cent. in the pyloric third. Ulcers are much more common on the posterior wall than on the anterior, where the incidence is only about 3 per cent. Six per cent. of ulcers occur at the cardia; 3 per cent. at the fundus, and 3 per cent, at the greater curvature. All these statistics are subject to wide variations. The outstanding feature is the preponderating frequency with which ulcers are found at the pyloric end.

Bauer believes that ulcer of the lesser curvature is found almost exclusively in the longitudinal folds known as the "gastric straits"—really a rudiment of the rumen. The pathogenesis of the ulcer is explained here on the basis that the rudimentary organs form a special site for morbid changes because the phylogenetic rest is not adapted to the functional peptic sphere. The mucous membrane of the strait is more fixed than that elsewhere, and its surface mass is less, hence it is more vulnerable.

Number.—These ulcers are usually single, but often multiple. Indeed, that they are commonly multiple is becoming more and more recognized. There were 34 in one of Berthold's cases and 60 in one of Hewitt's. Sometimes a perforated ulcer is found at operation and after healing another may perforate. In Brinton's 463 cases, 381 had one ulcer, 57 showed two

ulcers, 16 had three, 3 had four, 2 had five ulcers, and 4 had more than five. When multiple, they may all seem to be of the same duration, or some may be in a state of healing, while others seem to be quite recent. As a rule multiple ulcers are all acute. Welch and others regard 20 per cent. of cases as multiple. In 13 out of 21 cases operated on and resulting

FIG. 33

Two gastric ulcers: *A*, showing a shelving base and central perforation; *B*, more superficial.

fatally, Carless found more than one ulcer while Friedemann reports multiple ulcers in 45 per cent. of 230 cases of ulcer in which resection was done. These ulcers are sometimes widely separated, although usually near and at the pylorus, and along the lesser curvature. On this account he advocates wide resection. Sometimes one ulcer is in the stomach and

another in the duodenum. These "double" ulcers are said to occur in about 6 per cent. of all cases.

Shape.—The more acute ulcers are punched out in appearance, round or oval and sharp in outline, while the less acute ones are shelved or terraced, the widest diameter and the greatest loss of substance being at the mucosa. The ulcers become gradually narrower as one approaches the serosa (funnel-like, Aschoff). This corresponds to the distribution of the bloodvessels, and Orth drew attention to this fact. The still older lesions are often irregular in outline, spread out, and with the mucosa rolled inward and thickened at the edges. If extensive, they are serpiginous, especially where several have fused. Thickening and raising of the edges occur as the ulcer gets older. Often they are saucer-like, with bevelled edges, and rounded out or concave.

Various types of ulcer are described according to radiographic observations; thus, for example, there are: (1) The small round or oval ulcer; (2) the large crater-like, shallow, florid and indurated ulcer; (3) the deeply-penetrating ulcer; (4) the burrowing ulcer; (5) the mucosal or submucosal ulcer, and (6) the healed ulcer with contraction, which may be small or extensive, and which includes the hour-glass forms. It is questionable, however, whether all these differentiations have great value.

Size.—The usual size varies from 2 cm. to 3 to 4 cm. in diameter; in many instances they may be as small as 1 cm. or less, or as large as 10 cm. in diameter, sometimes even forming a ring more or less completely surrounding the organ. Peabody records one measuring 19 by 10 cm.

Histology.—The lesion is essentially a necrosis. There is very little inflammation or sign of healing in acute round ulcers, and even in many older ones; hence the slow repair, resembling somewhat the ulcus perforans pedis. There are, moreover, some signs of digestion.

Healing and Cicatrization.—Undoubtedly many ulcers occur and heal without giving symptoms of any kind. M. J. Stewart has discussed this subject. Autopsies showed scars as often as latent ulcers, and duodenal scars half as often as duodenal ulcers. There are four times as many single scars as multiple ones. Hour-glass contractions have been found in 6.5 per cent. of all healed ulcers. Many are superficial erosions rather than ulcers and healing occurs with granulations from the submucosa and scar formation. The frequent presence of scars and little fibroid areas suggests the probable existence of previous ulcer. The healing process commences from the sides and floor of the ulcer. There is proliferation of the adjoining fibrous and glandular tissues, the edges become indurated, and the margins are more indefinite and irregular in outline, with signs of puckering and contraction. The floor is usually smooth, grayish red, rarely ragged, and in old ulcers, there is an indolent granulation tissue or a definite scar. Adhesions externally and cicatrization internally induce stenosis and deformities of all kinds. The gland structures are repaired to a limited extent only; the new tubules are small and atypical, with cylindrical cells often arranged around the lumen, with no opening toward the stomach cavity and no secretion from the cells. Sometimes in old ulcers the healing process leaves chronic inflammatory areas which tend to erosion and recurrent bleeding. The area of stomach

around old ulcers is often infiltrated with small cells and fibroblasts to a great extent, in other words, a chronic gastritis. Where muscle tissue is lost it is replaced by fibrous tissue.

Scars vary in size, and, according to their size and situation, and to the amount of contraction which follows the healing process, they may or may not cause perceptible deformities and corresponding functional disturbance. The deformities comprise hour-glass contraction, pyloric stenosis and gastrectasis, and other irregularities with or without obstruction. Perforation occurs when the ulcer penetrates down to the serosa before adhesions have formed, and for this reason it naturally occurs most commonly on the anterior wall. On the other hand, penetrating ulcers may perforate the wall through adherent areas and reach adjacent viscera and tissues outside of the organ.

Symptoms.—Latency.—There may be no characteristic symptoms, and the first discovery of a gastric ulcer may be made unexpectedly at autopsy. Stoll found it latent in 27 per cent. of his autopsies; Lebert found that 15 per cent. of 110 cases were latent until severe symptoms arose. Then, again, the first evidence may be a sudden or perhaps fatal hemorrhage or perforation. It may be latent, even if perforation has taken place, as in one instance in which an ulcer giving suspicious signs of perforation remained quiescent. The patient for some days after the event seemed to improve, and there was little or no tenderness in the abdomen. Several weeks later an abscess developed in the pelvis, which was opened per vaginam and drained, and the autopsy revealed the origin to be in a fistulous opening from a perforated gastric ulcer. Sometimes nothing but *backache* occurs, as in the case of Beneke, in which for years this was the only symptom; a sudden peritonitis from perforation caused death and the autopsy showed old adhesions to the liver and a perforation between the adhesions into the abdominal cavity. Sometimes spinal disease is suspected, and a plaster jacket has been put on.

Dyspepsia.—As a rule, unless perforation or hemorrhage occur, the acute ulcers are not recognized as such, and there is a long period of intermittent dyspepsia before the symptoms and signs suggestive of ulcer are defined. While the cardinal signs are pain after eating, epigastric tenderness, vomiting, and hematemesis, yet often, perhaps even as a rule, the symptoms are less definite and *dyspepsia* is the only evidence to be found, with perhaps a little vomiting or regurgitation. There may be a sense of fulness, weight, or distention with gaseous eructations. With these there may be pyrosis, occurring during the digestive period, or mere gnawing or burning or "*heisshunger*" (from hyperacidity). Periodicity is almost pathognomonic. The general condition of the patient, as a rule, remains good, although anemia, emaciation, and weakness are common and sometimes marked as the duration is prolonged. Nervousness, melancholia, headache, and dizziness are frequent; so, too, are amenorrhœa and dysmenorrhœa. Fever is usually absent, unless complications arise (peritonitis, hemorrhage, etc.). Often there may be a rise of 1° without complications, perhaps associated with anemia. The appetite varies; it may be excessive, but the patient fears to eat because of the pain which follows soon upon temporary relief. Thirst is common. Constipation is the rule; the stools may show blood.

The urine is lessened in quantity when vomiting occurs or when less nourishment is taken. It is usually less acid than normal, especially when gastric hyperacidity is present. Indeed, it is often alkaline, particularly if gastrectasis be present, and then, if there is fermentation in the stomach, the urine shows an excess of ethereal sulphates and indican. Sometimes there is albumin and this is not uncommon after severe pain. Dreschfeld found albumoses occasionally present.

Special Symptoms.—*Pain.*—This may exist in all degrees from a slight discomfort, due to hyperacidity, to acute agonizing paroxysms. It may be relieved or aggravated by food. Pain occurs in over 90 per cent. of all cases. Intermittency of the pain is one of its most characteristic features. It is frequently localized and nearly always referred to the same spot in the epigastrium below the xiphoid cartilage. Pressure of the hand or clothing usually aggravates it. It may or may not be altered by a change of posture. One may say, as a general rule, that the effects of posture give no clue to the site of the ulcer.

Time of Appearance.—Pain occurs during the digestive period either at once after taking food, or at the height of digestion, two to four hours after; the hyperacidity and hypermotility increase it.

Site.—The pain is usually in the epigastrium—high up—and may be to the right or left of the median line, though the tenderness is more to the right side as a rule. According to French writers, two points of pain exist: (1) Visceral pain corresponding to the injured area, occurring late in the disease and only with perigastritis, and (2) solar pain—epigastric and not characteristic of ulcer; it is equally common in other diseases. Not infrequently a tender point is found in the back, 2 to 3 cm. to the left of the vertebral column, somewhere between the seventh to twelfth dorsal vertebræ. Bassler regards this as being referred from concomitant lymphangitis about the cœliac axis or from adhesions or irritability of the peritoneum from the affected area.

Effect of Food upon Pain.—It is distinctly aggravated by a large amount of solid food, but there are exceptions in which food sometimes gives relief, especially albuminous food, if there be hyperacidity. Sometimes there is no relation between the food ingested and the onset of the pain. Rutimeyer found this to be the case in 14 per cent. of his 200 cases. The pain is often relieved by rectal alimentation.

The *cause* of the pain varies, it being apparently due sometimes to food, or distention; sometimes to the gastric movements or to involvement of the peritoneum. Scars do not usually cause pain unless there are adhesions. J. Mackenzie holds that it is a viscero-sensory reflex—a referred pain—and that the tenderness depends on muscular and cutaneous conditions rather than on organic change in the stomach itself.

Vomiting is perhaps less constant than the pain. There may be merely nausea and flatulence without vomiting, or, again, the vomiting may be more or less frequent. It has a very definite relation to pain, by which it is usually preceded. It occurs sometimes immediately after taking food, but usually one, two, or three hours later, that is, during digestion and generally at its height. The pain is usually relieved by it. In some cases the vomiting may depend on infection from the mouth. In more or less

acute ulcer there are few if any signs of motor insufficiency, and the vomitus consists merely of the food taken; in the older ulcers, when perhaps pyloric obstruction has occurred and the stomach is dilated, the usual vomitus of motor insufficiency and gastrectasis may be present. As hyperacidity is usually present, one finds, as a rule, that digestion is quick and the albumins are well divided, although at other times the food is quite undigested and the vomitus sour from the pressure of organic acids.

Hematemesis.—Blood is frequently present in the vomitus, and occurred in more than 25 per cent. of all cases of gastric ulcer at the Royal Victoria Hospital. It is well to remember, in this connection, the many other causes of hematemesis that may exist, especially erosions of the mucosa. The source of the blood in gastric ulcer may be venous, arterial, or capillary. Savariaud found in 54 cases that the hemorrhage was venous in 4, from the splenic artery in 17, from the coronary artery in 6, from the pancreatico-duodenalis in 7, from the gastric arteries in 10, while in 10 others the source was undetermined. Sometimes the bleeding is more latent, not being visible to the naked eye either in the vomitus or feces, although minuter methods of detection reveal its presence. These "occult bleedings" have considerable importance in diagnosis.

One cannot always tell the actual vascular sources from the amount of blood. The hemorrhage may be severe or slight. It may be fatal at once, even before ejection from the stomach, the "hemorrhagie foudroyante," when a large artery is eroded; or there may be repeated small hemorrhages. Hemorrhage is responsible for about 20 per cent. of all the deaths in ulcer.

Symptoms and Signs of Hematemesis.—The hemorrhage comes on usually after meals, subsequent to some effort or strain, such as from vomiting or defecation. Usually when there is a serious hemorrhage, the patient vomits a large amount of bloody fluid, becomes pale, cold and clammy, complains of dizziness, is often semi-conscious or more or less collapsed. Headache and thirst follow. The pulse is rapid and small, and there is dyspnœa or sighing, and often complaint of a warm feeling in the epigastrium. If recovery occurs, the reaction is apt to come on with fever. The vomited blood may be bright or dark in color, bright if the vomiting be arterial, copious, and rapidly following upon the escape of the blood from the vessel, because the corpuscles are comparatively unchanged. It is more usually dark red, sometimes brown, resembling coffee-grounds, the hemoglobin having been changed to methemoglobin by the hydrochloric acid, and few corpuscles are left unaltered. The vomitus, which may be copious, contains coagula, bits of food, is usually acid in reaction, and devoid of froth. There may be lesser repetitions of the hemorrhage, or after the one large one there may be spontaneous cessation. The stools are almost invariably darkly discolored from the passage downward of some of the blood. Hemorrhage may be divided into that from the acute and that from the chronic ulcer.

In the *acute ulcer* there may be a spontaneous, abrupt, and alarming onset, without previous warning and history. Much blood is lost quickly, and the patient either soon dies or the hemorrhage ceases of itself, with only slight repetitions and with anemia; or there may be an abrupt

onset, with short intermissions before one or more recurrences. In *chronic ulcer*, the hemorrhage varies much. There is a history of chronic indigestion for some time previously, and of persistent anemia.

Moynihan divided these cases into four groups: (1) The hemorrhages which are latent and insignificant. (2) Those which are intermittent, infrequent, and moderate in amount. There is no danger in these of a fatal issue. (3) Those which have become worse after the symptoms have developed. The bleeding may be copious and repeated, and, therefore, perilous, perhaps even fatal. (4) Those cases in which the hemorrhage is sudden, overwhelming, and fatal. Sometimes the hemorrhage is repeated in spite of care, and, according to Moynihan, is attributable to distention of the stomach and stretching of the ulcer. It does not, apparently, require a great deal of blood to produce a tarry stool, although Hosslin, quoted by Howard, states that 500 cc. are necessary. Sometimes the color is brighter, depending on the freshness of the blood, the amount, the rapidity of bleeding, and on its passing with the intestinal contents. The discoloration is due to the intimate mixing of the blood and chyme in the small intestines. Sometimes all the blood escapes per rectum, and there is no hematemesis; this occurs when the bleeding is more gradual or the ulcer near the duodenum.

"*Occult Bleeding.*"—Strauss first drew attention to this valuable sign, and, in 1902, Boas showed the diagnostic significance of examining the gastric contents, vomitus, and feces for evidences of hemorrhage. It is well-recognized too that much blood may be present in the feces and yet go undetected by the unaided eye.

The examination for occult hemorrhages must be preceded by the exclusion of all other sources of blood, *e. g.*, food containing blood, bleeding from the gums or nose, injuries to the gastric or œsophageal mucous membrane from passing a tube, general or systemic diseases, and diseases of the digestive organs. Of the general systemic diseases, one considers especially hemophilia, purpura, scurvy, typhoid fever, arteriosclerosis, and tabes with gastric crises. There are two other classes of diseases of the alimentary tract in which this sign may appear and give rise to some confusion in the diagnosis: (1) Malignant tumors of the gastro-intestinal tract and of the pancreas or liver with ulceration, and also hemorrhagic pancreatitis. These give marked and often constant reactions. (2) Stenosing gastritis, alcoholic gastritis, polypi, intestinal parasites, tuberculosis, syphilitic or simple catarrhal ulceration of the bowel—also hemorrhoids, fistula, and fissure. All of these give constant and marked reactions. The ingestion of raw or ill-cooked beef (200 gm.), blood sausage, etc., gives positive reactions.

A "meat-free" diet is recommended as a preliminary to the test, and if this be carried out thoroughly for several days, the results are more accurate. Brown and Gaither agree with Boas that for this reason, all meats, fish, oysters, chicken, green salads, chocolate, cocoa and red wine should be excluded from the diet. Purgation, too, must be avoided. Lacto-farinaceous foods and eggs are usually employed for the test diet.

The Benzidin Test.—This is probably the most suitable of all the chemical tests for occult bleeding. First used by the Alders in 1904,

benzidin, one of the diphenyl group, has been recognized as one of the most delicate tests hitherto employed for the detection of occult blood, giving positive results in blood dilutions of 0.001 per cent. The purity of the benzidin is of importance for its delicacy of reaction.

Technique.—Make up a fresh saturated solution of pure benzidin in 2 cc. of glacial acetic acid. Add to this an equal amount of H_2O_2 (3 per cent.), and the appearance of watered silk will indicate a satisfactory dilution. Overlay this mixture with 1 cc. of a boiled watery solution of a portion of the feces, and the reaction, if positive (*i. e.*, a blue or green color at the line of contact) should occur within thirty seconds. The depth of color and speed of reaction occur in direct proportion to the amount of blood pigment present.

Limitations in the value of the test must be emphasized. Apart from the sources of error above noted in respect of disease and foods, it is important to remember that sweat and saliva may yield positive reactions, as also certain chlorophyll-containing vegetables if unboiled.

The Value of Tests for Occult Blood.—The value of the test depends entirely upon the degree of care with which it is carried out. After satisfactory exclusion of all extraneous sources of the blood and after elimination of factors possibly confusing the interpretation of the test, a positive result suggests a lesion of the mucosa in the alimentary canal, and three tests in succession must be made. If the mouth and the rectum be excluded as a source, the lesion is more limited still. When no evidence of inflammatory disease exists, *e. g.*, enteritis, and when no general disease is found (*e. g.*, cardiac or hepatic), a positive test for occult blood suggests ulceration—benign or malignant. Repeated positive tests occur more usually in cancer; the persistence of negative findings strongly suggests the absence of any malignant disease of the alimentary canal. Negative tests, however, do not exclude a diagnosis of ulcer. The prognosis of ulcer depends to some degree on the results of occult blood tests, for the recurrent presence means imperfect healing.

Signs.—But little is to be gained from physical examination of the abdomen in acute ulcer. Tenderness is a common finding and yet the clinician who attaches too much importance to it alone is liable to be surprised and disappointed at an exploratory laparotomy. The tender point is often localized in the epigastrium, sometimes more diffuse. In pyloric ulcer it is apt to be in the right hypochondrium, though no rule obtains. No tumor is palpable in fresh ulcer. In older ulcers which have become callous or when scarring has occurred and caused pyloric obstruction or deformities in the stomach, the objective signs may be much more marked. Peristaltic movements, perhaps a dilated stomach, may be seen on inspection, while palpation may reveal a tumor of varying size, more or less movable, according to its situation and the presence of adhesions, usually at some part of the upper abdomen. The palpable mass represents the thickened ulcer itself, muscular hypertrophy or adhesions, or may be due to fibromatosis (A. Thompson).

Gastric Analysis.—This varies according to the type of the ulcer. In the acute forms the examination of gastric contents may show little that is abnormal. The hydrochloric acid may be normal in amount, the

proteolytic digestion unimpaired, and the motor power good. At other times there may be hyperacidity with hypersecretion, or the reverse, and motor insufficiency may be evident. Blood is often present, and may be visible to the naked eye or found only by microscopic or chemical examination. In the more chronic forms the findings will depend on the site of the scarring ulcer. If pyloric stenosis is present, there is usually hypersecretion with retention of food, good digestion of proteins, and little or no change in the carbohydrates. Sarcinæ are usually found in such cases, and also yeast cells in abundance. Blood, either evident or occult, is common. Lactic acid is present only when there is stagnation and hypochlorhydria. Rutimeyer found motor insufficiency of the first or second degree in 42 per cent. of his cases.

Experience has not shown that a chemical examination of the gastric contents is of more than an adjunct value in the diagnosis of ulcer. The variations in the acidity and the fact that hyperacidity exists in only about half of all ulcer cases, render this test of minor importance.

Rehfuss, by fractional analysis, presents the secretory findings as a curve made by plotting the free and total acid values as ordinates against the time relations as abscissæ—specimens being drawn every fifteen minutes for two hours. The amount of chyme remaining at the end of two hours is taken as an index of the motor power. Carlson's work demonstrates the fallacy of building up a pathology of the stomach on acid values alone. Inasmuch as the pepsin keeps pace with the acid, the value of digestive tests is also minimal.

The finding of blood in the gastric contents is only of value if there is more blood present than a mere streaking, for this latter occurs very frequently through trauma in the passing of the tube.

Roentgen-ray Examination.—*Radiography*, with more perfected technique, has replaced chemical analysis in the diagnosis of ulcer.

The work of many radiographers has shown that no better test for ulcer exists than the study by radiology. Its fallibility, however, must be recognized, and many deformities arising from disturbances of motor function create false impressions. Frequent and repeated observations are necessary before one may come to a definite diagnosis in such cases. It is further clear that a differentiation of the site of an ulcer as between the stomach and the duodenum is not always easy. The recognition of the pyloric vein as the dividing line between the stomach and duodenum, as employed by the surgeons, does not hold true in all cases observed by the roentgen-rays. It is important to realize that in every roentgen-ray examination, certain fundamental principles are imperative:

1. A careful clinical history must always be considered with the report.
2. Examination by the fluoroscope is far more important than the mere skiagram.
3. Physical examination is essential, and more particularly palpation under the screen.
4. Skiagrams are mere adjuncts to the diagnosis and the serial pictures are more important than the single ones.
5. Negative findings do not exclude ulcer.

A persistent, careful, conservative roentgen-ray examination, with

these adjuncts, may give a positive diagnosis in, perhaps, 90 per cent. of cases; in the other 10 per cent. diagnosis still remains in doubt.

Method.—The method employed in the Royal Victoria Hospital is that of the double meal. A drink of 3 ounces of barium sulphate in 12 ounces of milk, which is fluid, finely-divided and potable, is given six hours before the examination as a test of the gastric motility. The second drink is given at and during the fluoroscopic examination to determine the evidence of ulcer. The radiographic signs of ulcer are divided into direct and indirect signs

1. The indirect signs of ulcer refer to the changes in position, size, shape and outline of the stomach, its mobility, peristalsis, peristole, its tonus (during deglutition and how the food is held at the funnel in the fundus and how it drops below). The fluoroscope is of especial importance in a prolonged view of the action of the stomach under the immediate influence of the meal. Manual palpation of the stomach under the screen adds much information as regards the site of the pain and its correlation with local evidence of disease. Palpation further increases the value of the indirect signs, more especially as regards the filling of the bulb.

The indirect or secondary signs are chiefly of value when the ulcer is too small, shallow, indefinite, or concealed, to be seen by fluoroscope or film; these, with the clinical findings and history, aid a positive diagnosis materially. Of all these signs, the incisura is the most important evidence; it arises from a spasm of the circular muscle in the plane of the ulcer, forming an indentation in the curvature opposite. As the ulcer is usually on the lesser curvature, the indentation is usually found in the greater curvature. The indent may be small or large, deep or shallow, single or multiple: it is most easily recognized when the barium is seen coming to a point and then gradually filling the remaining lower portion of the stomach. Manual pressure upward brings it into view. Confusion often arises from functional spasm due to intra- or extra-gastric causes, normal or abnormal; these, however, are more transient, while the incisura is constant and stationary; it survives manipulation and the administration of antispasmodics.

Hour-glass contraction, while a frequent sign in chronic ulcer, is commonly but a functional condition which one is apt to confuse with an organic disease.

The Six-hour Residue. This occurs in more than half of all gastric ulcers. This stasis is assumed to be due in the early stages to a disturbance in peristalsis with pyloric spasm, hyperacidity and hypomotility. It depends, however, upon the type or habitus of the individual, and normal variations in the expulsion time of food from the stomach have very wide limits. A hypotonic, left-sided stomach is common in gastric ulcer, all the more so if not conforming to the patient's habitus.

Lessened mobility depends on the form and position of the stomach and the relaxation of the gastric wall. It is due to many causes, often extra-gastric, and is of minor importance. Palpation under the screen of a local tender point found by physical examination is sometimes of value over a suspected area, but is by no means pathognomonic.

2. The direct signs are those concerned with the local anatomical and

functional changes. From this diagnostic standpoint, four types of ulcer may be considered:

1. The erosion.
2. The penetrating ulcer.
3. The perforated ulcer, with or without an accessory pocket.
4. The carcinomatous ulcer.

1. The erosion cannot be determined by roentgen-rays unless a persistence of barium is seen in it, or unless it is accompanied by a constant incisura opposite to it, due to spasm. Gastric hypotonus, with six hours delay, due to pyloric spasm, adds to the suspicion of ulcer. This spasm may occur even if the ulcer is far from the pylorus but similar spasms can occur through nervous action alone. All these suggestive signs of ulcer are usually significant, only if there be confirmatory clinical evidence.

The other three varieties represent chronic types of ulcer and are variously classified with reference to their objective signs. The deformities are the chief pathognomonic or immediate signs. They are many and varied. Normally, the lumenal content is even, except on the perpendicular edge of the greater curvature where the descending colon or ascending part of the transverse colon very often make an irregularity in the upright posture.

With ulcer, the deformities include: i, The niche; ii, the pocket; iii, the cauliflower-like perforation; iv, the induration; v, the slight excavation; vi, the hour-glass stomach.

These deformities may arise from perigastric adhesions, from scars, perforations, spasticities or pressure of neighboring viscera.

(i) The *niche* consists of a projection from the shadow of the gastric lumen, *i. e.*, a filling of the ulcer crater with barium, and there is often an air bubble above. The niche may occur anywhere, although most commonly on the lesser curvature and the posterior wall, where it is best seen in the oblique position. Sometimes, though a niche exists, it may be filled with mucus, which prevents the barium from entering, and this gives a negative result. Carman and others commend the use of a small barium and water drink to outline the gastric rugæ and their convergence toward an ulcer. In the profile view of the niche, it is often more easily seen, even when quite minute, and simultaneously there is often prepyloric contraction, which, however, must be stationary and persistent to be of diagnostic value.

(ii) The *accessory pocket* results from perforation into the surrounding organs or tissues, and varies in size and shape, and may or may not have a demonstrable connection with the gastric lumen. The barium remains in it when the rest of the contents have passed on. Its mobility varies with the site and the organ invaded. It usually shows a fluid level and a bubble of gas above.

(iii) The *deformed stomach*. Cicatricial contractions, perigastric adhesions, hour-glass stomach and infiltration of the wall induce various deformities, altering the shape, site, size and mobility of the stomach. In contradistinction to cancer, one may say that the ulcer usually increases the lumen of the stomach, while cancer lessens it. It is said that an ulcer, with a niche of 3 cm. or more in diameter, is probably cancerous in nature.

Diagnosis.- J. B. Murphy's epigrammatic advice with reference to the treatment of ulcer, *viz.*, "First catch your ulcer" was not without its significance. The diagnosis in acute ulcers is so often dubious and incapable of proof that experiences gathered from past statistics are but a poor guide for either diagnosis or treatment.

A certain proportion of ulcers are latent and the ordinary symptoms in gastric ulcer are applicable to most disorders of the stomach and dependent, not upon the ulcer itself, but upon the accompanying disturbances of gastric function. Thus, for example, flatulence, nausea, vomiting, cachexia, pain after food and its recurrence are symptoms not of the ulcer itself but of the pyloric spasm, hypersecretion and other disturbances of function. Similar conditions may arise with cholecystitis, appendicitis, renal calculi, and certain organic nerve diseases, so that a differential diagnosis must be made with care. It is generally conceded that in early youth symptoms such as the above are in most cases extra-gastric in origin, most commonly from the appendix. Unless, then, other factors are added to the history and examination, no conclusion should be reached. Even if hematemesis or melena occur, the diagnosis should still be made with care although the suspicion of ulcer will be augmented. Hemorrhagic erosions of the stomach are not infrequently associated with appendicitis.

Physical Examination.—Tenderness alone is very apt to deceive, and unless controlled by fluoroscopic examination as to the site and functional relations, it is not to be considered an infallible sign. The abdominal examination gives no other clue of importance in acute ulcer. In the chronic forms, on the other hand, information is gained chiefly through the anatomical lesion present and the deformities or the sequelæ which may have been induced thereby.

The value of *gastric analysis* is limited, and apart from the presence of blood and of hypersecretion (which are, after all, only adjuncts to the diagnosis), they do not furnish very reliable data.

Einhorn invented a duodenal bucket attached to a long silk thread, and Bassler a somewhat similar "string" test, the object in each case being to detect the presence of an ulcer and possibly its location by means of the blood stain, or brown-black discoloration on the string, from contact with the eroded surface of the ulcer. The bucket or shoe button, or B. B. shot with string (No. 8 braided silk) attached and of known length, is swallowed in the evening and is removed in the early morning and examined for any stain on the string. The situation of the stain on the string, measured, according to its distance from the incisor teeth, determines the site of the lesion. Bassler warmly recommends this method for the diagnosis and prognosis of ulcer of the cardia or pylorus, but not of the fundus or greater curvature.

In the more *chronic cases* diagnosis depends especially on the anamnesis and physical signs, and much assistance is often gained through the use of the fluorescent screen and the skiagram. The history of pain, more or less intermittent, localized, and accompanied by tenderness, the recurrence of vomiting, sometimes with blood, the absence of marked and progressive emaciation, the frequent hypersecretion, all point to ulcer. Sometimes with these signs the scarred ulcer is palpable as a tumor.

Differential Diagnosis.—One must differentiate between ulcer and many other conditions, among which may be mentioned gastralgia, hyperesthesia, hysteria and simple hypersecretion, pylorospasm, gastritis, cancer, cholecystitis and cholelithiasis, renal calculus, pancreatitis, aneurism of the abdominal aorta, and even spinal disease and tabes with gastric crises. In most of these conditions the careful consideration of the anamnesis with the physical findings make clear the underlying disease. In some, however, the differentiation is not so easy.

Gastralgia.—In this there is paroxysmal pain, not directly excited by food, nor related to or regularly affected by its ingestion. Pressure often relieves the pain; there are no tender points. If there be vomiting (and usually this is inconstant and irregular in onset), it does not necessarily give relief to the pain. Digestion is normal, and milk or other bland diets are of little use in the treatment. Aerophagia and eructations of gas are common. Neurasthenic symptoms and mucous colitis are often superadded. Epigastric pulsation is common. Hematemesis and occult blood are absent. Gastralgia often accompanies *uremia* but the other signs give the diagnosis.

Gastritis.—A cause is present; the pain is more diffuse, less severe, and not increased much on pressure. The tongue is foul and coated. The vomitus contains much mucus, often organic acids, and there is usually diminution in the amount of free hydrochloric acid. If blood be present it is rarely large in quantity. Certain cases of gastritis with hemorrhage are at times indistinguishable from ulcer.

Cancer.—Debility and emaciation often precede the other signs; the pain is more constant and more independent of food, is often nocturnal, though it may at times be quite absent, and there may be simply a discomfort. There is anorexia, as a rule; vomiting, which is common, gives less relief than in ulcer. The vomitus is rather that of motor insufficiency, and shows little or no hydrochloric acid, but usually some lactic acid, and other evidences of fermentation in the odor and in the presence of ill-digested food and the Boas-Oppler bacilli. Any hematemesis has more the character of coffee-ground vomitus. Occult bleedings are more constantly found than in ulcer. The case is somewhat different when ulcer exists as a pyloric tumor with dilatation of the stomach, or when a cancerous growth has been engrafted upon a previous ulcer. Cancer limited to the pylorus is rare; the onset is obstructive, with vomiting, cramps, and emaciation, in a more elderly person; the course is progressive, and dietetic treatment affords no relief. If first seen when dilatation is really pronounced, the diagnosis must be made chiefly from the history and by examination of the gastric contents and stools. Free hydrochloric acid is absent in 90 per cent. of these cases and lactic acid is evident. With ulcer there is usually hyperchlorhydria, or a normal amount of hydrochloric acid. The history of ulcer causing dilatation is of years' duration. The appetite improves with lavage, as does also the general condition. When there is a cancer engrafted upon an old ulcer, there is increase in the pain, especially if there be some emaciation and weakness; the hydrochloric acid is gradually lessened; and the tumor increasing in size assumes a more nodular character. The roentgen-ray will show a filling defect and other features mentioned.

Appendicitis.—Appendicitis is, perhaps, more often confused with ulcer than with many other organic lesions. In 19 of 51 of Moynihan's cases this mistake had been made. Today, the error should not be so frequent. A special note of the history of the onset is important, as also the location of the early objective signs below the umbilicus. Radiography usually determines the difference.

Gall-stones.—The differential diagnosis is often extremely difficult, and in a number of cases quite impossible for the time being. This is especially the case when the ulcer lies at the pylorus or is in the duodenum. There may be persistent pain, as in ulcer, especially after the taking of food, and with it vomiting; the vomiting may give relief; there may be tender points, and upon careful treatment even the symptoms may for the time disappear, and all this without jaundice, bile in the urine, or other signs of gall-stones. As a rule, however, there is sudden, colicky pain at any time, of great severity and subsiding suddenly, as also tenderness in the right hypochondrium, slight fever, and perhaps sweating. Retching and vomiting occur with the pain and give no relief, pain continuing long after the stomach is empty. There are intervals of health and normal digestion. The coexisting gastralgia may be paroxysmal, and there is often hyperacidity. Not infrequently the sclerotics are subicteroid and a trace of bile may be found in the urine. Even with radiography, the diagnosis is often uncertain. Many cases of duodenal ulcer are found with gall-stones. Deformities which occur in the bulb as a result of adhesions outside of the gall-bladder and of the pylorus render the diagnosis extremely difficult, and laparotomy alone is often the only means of differential diagnosis.

Complications and Sequelæ.—The most important are: perforative peritonitis, perigastritis (suppurative and adhesive), subphrenic abscess, fistula between the stomach and adjacent organs, abscess of the liver, chronic hepatitis, acute and chronic pancreatitis, constriction of the bile-duct with jaundice, cardiac stenosis, pyloric stenosis, deformities of the stomach with dilatation or hour-glass stomach, cancer of the stomach, general emphysema, parotitis (sometimes with perforation and sometimes after hemorrhage), tetany, hemorrhage, anemia, etc.

Perigastritis.—As a result of chronic ulcer, peritoneal reaction occurs in the vicinity, and may be infectious in origin. The resulting inflammation may be suppurative or merely adhesive. Adhesions occur to neighboring organs or to the parietal peritoneum, and symptoms are thus produced which may give a clue to the diagnosis of the complicating condition. Surgical experience indicates that these are extremely common. The adhesions form most commonly about the lesser curvature, in the mid-region in front and behind, where the parts, too, are most at rest; also at the extreme ends of the organ, cardia and pylorus, described by the French writers as precardiac and prepyloric perigastritis. They are firm, well organized, and thick, and extend well beyond the limits of the ulcer and in extreme conditions even to the pelvis. With pyloric ulcers the gall-bladder and liver may be firmly bound to the stomach and gastrectasis thus commonly ensues. Sometimes an hour-glass stomach is formed often with penetrating ulcers. The *x*-rays have shed much light on these cases. The ulcer very frequently penetrates

deep into the adherent parts, forming tracts with expansion at the end, in which the bismuth shade is constant for days following the meal.

The Symptoms.—The location and degree of adhesions, as well as the type of inflammation, determine the course and special symptoms. The special features are pain, tenderness, and chronicity, without either cure or markedly progressive failure of health. Gall-stones, angio-cholecystitis or cancer, may simulate the condition or a secondary pyloric stenosis, or the perigastritis may be a mere accompaniment of a neighboring disease. Signs of ulcer have usually been present for a long time previously, and to these are added exacerbations of the *gastralgic pains* often radiating to the back or upward, only to some extent relieved by rest, and increased on forcible straightening of the trunk. Ingestion of food or fasting has no lasting effect on the symptoms. Examination reveals perhaps nothing but tenderness, or there may be increased resistance and even a definite mass, which is subcostal, perhaps superficial.

The differential points are briefly: A previous ulcer or one still unhealed, with a history of long standing and yet an absence of cachexia and metastases; perhaps gastrectasis; persistent pains more or less influenced by posture and sudden exertion; localized tenderness; occasional jaundice without involvement of the liver; periodical febrile attacks of short duration. Gastric analysis gives no distinctive results. The roentgen-rays are of great value here, revealing frequently a perforating ulcer with fixation of the viscus from perigastric inflammation.

Perforation.—This is one of the most serious complications of gastric ulcer, and occurs in a varying percentage of cases (1 per cent., Leube to 18 per cent., English). Clinically, in 1336 cases there were 45 perforations, *i. e.*, 3.4 per cent. In 1615 autopsy cases there were 336 perforations, *i. e.*, 22 per cent. Perforation rarely occurs before the age of twenty years. Lee and Wells, in a careful search of the literature over a period of thirty-five years, find only 160 cases occurring during the first ten years of life. In the first year there were 8 cases, and out of their own experience, they record 1 case of perforation *in utero*. *Sex.* In Gibson's series, there were 56 males and 4 females. *Site.* According to Stewart and Barber, 76 per cent. occur within the pyloric sphincter, the size varying from a pinhead to $1\frac{1}{2}$ cm. *General peritonitis* occurs chiefly when the perforation takes place rapidly before adhesions form. The extent depends upon the time from onset, for the transverse colon and the mesocolon act as temporary barriers for a few hours before extension occurs into the lower half of the peritoneal cavity (Berg). Perforation of a gastric ulcer sets up a general peritonitis more commonly than does a duodenal ulcer, perhaps because the duodenal contents are more sterile, or because there are more chances of adhesions. The same rule applies to pyloric ulcers as compared with ulcers elsewhere in the stomach. The amount of soiling depends upon the duration of the perforation, the size of the rupture and the motility of the stomach and its contents.

Course of Perforated Ulcer.—Sometimes, though rarely, an acute perforative general peritonitis may heal spontaneously. This is extremely rare in the acute cases. Some subacute and chronic cases recover, although usually with conditions which lead to more or less chronic

invalidism. *Extension* may occur in almost any direction. Perforation into the liver or pancreas may occur with abscess or chronic inflammation in either organ. There may be obstructive jaundice with pressure on or stricture of the ducts and a *catarrhal cholangitis*. Subphrenic abscess may occur, and was due to ulcer in 20 per cent. of 179 cases (Maydl). The *portal vein* is sometimes invaded, and pylephlebitis follows. The gall-bladder may be involved and stones may fall into the stomach through the fistulous opening. Sometimes the *spleen* is involved, and we may find a perisplenitis. If the perforation penetrates the *intestines*, there may be a severe diarrhœa and bloody or purulent feces or fecal vomiting. A gastro-colic fistula may form; Murchison found 10 cases of this in 33 perforations due to ulcer.

Rarely perforation occurs into the *abdominal wall* with an external fistula. In the more chronic cases sometimes the perforation occurs at a place far distant from the original ulcer, by dissecting and pointing, as in one instance in which a pelvic abscess formed and was drained through the vagina some weeks after the perforation of the ulcer.

The Symptoms and Signs of Perforation.—The early signs are the most characteristic, hence the importance of seeing cases early, but there are no pathognomonic symptoms previous to perforation. The onset is usually sudden; indeed, the sudden pain or other distress may be the only sign of the ulcer, though a careful anamnesis is of the greatest importance in the diagnosis. English found no history of stomach trouble for some time before perforation in 11 of 50 perforation cases. The patient need not be overcome and incapacitated at once; sometimes he is able to walk into the hospital with such a perforation. In one case under Seymour Taylor's charge there was a single bloody stool as the only sign of perforation, without pain or abdominal signs of any kind, and a fatal result ensued with no other local development. It commonly follows some strain, such as vomiting, trauma, or a hearty meal.

Pain is the earliest symptom, is not only sudden but of great severity, usually referred to the epigastrium and spreading soon to the right and left, but not leaving its original site. Attention has been drawn to the severe pain which occurs in the left supraclavicular fossa, coming on within a few minutes of perforation and lasting but a short time. Dyspnœa soon follows, and deep breathing causes pain about the diaphragm, so that these cases are sometimes mistaken for acute pleurisy. Vomiting is not so infrequent as was formerly thought; a small opening does not allow escape of so much contents—though with the gradually developing peritonitis, the cessation of a previously existing vomiting is very suggestive of perforation. Collapse and prostration supervene. In some cases remarkably little prostration is observed, which is apt to mislead, especially as the general signs may greatly improve after a few hours before graver symptoms develop. The degree of collapse depends in large measure on the amount and extent of the extravasation. The face is anxious, often pinched, and there is apt to be great restlessness. The pulse is usually accelerated, though sometimes it is normal, and the temperature may be but little altered immediately after perforation. Usually there is slight fever.

The *abdomen* may be flat and tense, sometimes it is distended; the muscles are rigid, often in the upper zone only, and there is diminished mobility, two signs of greatest significance. Tenderness is chiefly about the epigastrium and hypochondrium. Eighteen out of a series of 49 cases were diagnosed as appendicitis. Percussion may or may not give dulness here, and the liver dulness need not be obliterated, although this depends in great measure on the escape of gas into the surrounding parts. The sign of obliteration of the liver dulness is unreliable. Even when absence of liver dulness exists as far back as the midaxillary line, it may imply no abnormality. Nor, again, is it true that well-marked stomach tympany in the left hypochondrium excludes the possibility of perforation. A valvular perforative opening may exist allowing distention. On auscultation, a friction rub may be heard over the diaphragm, and sometimes the gurgling of fluid through the perforation.

Pseudo-perforation is not uncommon, *i. e.*, the signs and symptoms of perforation without other anatomical lesion than ulcer, as in a case recorded by Manges, in which a woman, aged twenty-seven years, after previous signs of ulcer (hematemesis, etc.), suddenly had pain and tenderness in the epigastrium, with a temperature of 102°, pulse 120 to 140, and marked rigidity. At operation no perforation and no peritonitis were found, simply the uncomplicated gastric ulcer. Leukocytosis varies in this as it does in the perforation following typhoid fever. We are told that attention should be paid to the base of the thorax on the left side, where one often obtains restricted movement, localized pain, and tenderness, with dulness in the lower axillary region and other signs of fluid (Osler). Fluid may collect beneath the diaphragm about the anterior and external surface of the spleen, or in the lesser peritoneum, and later the usual signs of general peritonitis may develop.

Cancer Developing upon Ulcer.—Cruveilhier first suggested this possibility in 1835, although he believed a cancerous diathesis essential to its development, and Rokitansky, in 1839, added further observations on its probable concurrence. Mayo, Moynihan, Panchet and Choyce all lean to the belief that ulcers of the stomach are potentially malignant. Clinical evidence is held to exist from the long history of some cancer cases and the fact that males are chiefly affected. Pathological proof exists in the fact that cancer commonly occurs in the stomach at the same situation as does ulcer, and Choyce in 69 specimens removed by operation found 22 in which the appearances suggested origin from ulcer. Furthermore, 11 in 165 resected ulcers were unexpectedly found to be cancerous.

Any dogmatic statement on the origin of cancer from ulcer seems impossible with our present knowledge, and other methods of deciding this dubious point must be looked for. Clinical histories seem to point to the possibility in some instances and a definite anamnesis applicable to such a transition exists. It must be admitted, however, that a history of gastric trouble prior to cancer does not mean a pre-existent ulcer, and, on the other hand, many cancers may grow slowly over a period of years before declaring themselves, and thus perhaps the so-called transition period was one in which cancer alone was present from the start, though without showing clinical evidence. Paterson pointed out the infrequency

of duodenal cancer in spite of the increasing records of ulcer in that location, and that ulcers left alone after short circuiting rarely show cancerous change. Friedenwald's statistics show but a small proportion of cancers arising from gastric ulcer (7 per cent.).

The Symptoms and Diagnosis of Cancer Forming on a Previous Ulcer.—The transition period between the signs of the original ulcer and the onset of the cancer varies greatly. There are some undoubted cases and the duration of symptoms in these has varied; it is sometimes short, or, in others, years have elapsed since the ulcer first formed. Malignant development is suspected when loss of weight persists with a cachexia greater than a mere ulcer would justify. In such cases, too, there is more constant pain, although perhaps even less intense, and its character alters to a more dull, sickening ache. Tenderness is more diffuse. There is more nausea and vomiting; at all events, the vomiting is more regular, and even if a longer time intervenes between the attacks, it is more copious and rancid, and readily excited by liquid food. Blood appears more frequently in the vomitus, and in small amounts; and occult blood is more constant in the feces. The appetite usually becomes less, the patient is more languid and weak, and is markedly anemic. The gastric analysis is not always characteristic of cancer and then only late in the disease, and often hyperacidity is present to the end. Mechanical and medical treatment are without avail, and if, with proper ulcer treatment, there is increase of the symptoms, especially emaciation, pain, vomiting, anemia, and weakness, cancer may be suspected.

Parotitis.—This is not common. S. Paget and Hone mentioned several cases in 1897, and English reported 5 instances among 50 cases with bilateral parotitis. Sometimes suppuration occurs. The condition probably arises in the same manner as in other diseases of the abdominal and pelvic viscera. Rolleston and others, while dubious as to its causation, do not regard it as arising from infection of Stenson's duct.

Tetany.—(See under "Motor Insufficiency or Gastrectasis"). This, while commonly associated with old scarred ulcers with dilatation, sometimes occurs without any such complication. There are mild and severe grades, the former with mere cramps and paresthesias at times, the more severe forms often resulting fatally. Albu reported 31 deaths out of 40 cases. Any source of irritation may induce an attack, and not infrequently lavage of the stomach which so often relieves the symptoms may at other time precipitate an attack. The tetany is supposed to arise from loss of salts or acids in consequence of prolonged vomiting. There is marked reduction in the calcium content of the blood. The peripheral motor neurones are acted upon. The work of Collip has revealed in Parathyrin a cure in many cases.

Pyloric Stenosis with Dilatation.—(See article on Gastrectasis and Motor Insufficiency.) Dilatation is fairly common and is associated either with pyloric stenosis from a scarred ulcer or perigastric adhesions as direct causes, or with contraction or spasm of the pylorus and mechanical irritation as indirect causes.

Cardiac Stenosis.—This may occur from cicatrized ulcers at the cardiac end of the stomach as also diverticula at various portions from similar causes, or through traction of perigastric adhesions.

Hour-glass Contraction of the Stomach. This is much commoner than was supposed formerly, largely owing to the findings in surgery and by the roentgen-rays. It consists of a contraction anywhere between the cardia and the pylorus dividing the stomach into two or more portions; sometimes it is trilocular. Moynihan described a case with four sacs.

Etiology. The condition is rarely congenital. Moynihan denies any such origin and deals with instances, which he claims are inaccurately described as congenital, regarding it as almost always dependent on some organic disease from ulcer, perigastric adhesions, or carcinoma. Nevertheless, in one specimen in the McGill Museum removed from an infant, the condition is so marked as to leave no other conclusion than that it was congenital. The direct and most common cause is an old ulcer with cicatrix or adhesions of the stomach wall or other parts, or both, or the formation of independent bands of fibrous tissue. Among 48 cases

FIG. 34

Hour-glass contraction of the stomach: *A*, cardiac portion; *B*, pyloric portion.

reported by Robson and Moynihan in 1906, 41 were due to ulcer. Other cases are not infrequently associated with cancer of the stomach, while tuberculous peritonitis may cause bands of fibrous tissue to form about the stomach and produce identical results.

The *symptoms* are at times quite indefinite, and at other times appear to be quite characteristic. They apparently depend on the original cause at first, but later the effect may be diagnosed, provided one exercises sufficient care and patience. As has been pointed out by others, the main symptoms are pain after meals, vomiting of stomach contents and sometimes also of blood, emaciation, and the presence of a tumor, due to cicatrization of old ulcers, with an absence of secondary nodes and of ascites. The condition is naturally associated with symptoms for many years, and the patients suffer much. For a time the symptoms seem to simulate stenosis of the pylorus, the presence of pathognomonic

features depending largely on the site of the contraction. This, as a rule, lies four inches from the pylorus, and therefore simulates pyloric obstruction with dilatation, all the more so as hyperacidity usually coexists and the *secondary cavity* is small. Moynihan gives the following sets of symptoms, the result of the experience of various authors: *First*, in lavage of the stomach, all the fluid fails to return, some, which is in the secondary pouch, being apparently lost (Woelfer's first sign); *second*, after lavage has apparently thoroughly cleaned the stomach, more contents reappear, probably foul and evil-smelling, the washings thus being again dirty (Woelfer's second sign), or the same may be found on withdrawing the tube after washing the stomach clean and then passing it again; *third*, the sign of paradoxical dilatation (Jaworski); this consists in the succussion splash on palpation after apparent removal of all the gastric contents, a sign which is of course present because only the cardiac sac is emptied; *fourth*, after percussing out the stomach and then distending it, a change in the position of the distension tumor is found at times. First the proximal pouch is distended and then the distal, and the notch is often visible between the two tumors when both parts are dilated (von Eiselsberg); bubbling and sizzling are distinguished at a point distinct from the pylorus on dilatation (von Eiselsberg), and patients are sometimes themselves conscious of this and of food passing from one pouch to the other. The roentgen-rays are by far the most satisfactory means of diagnosis revealing the double pouch with intervening constriction which persists.

Course and Prognosis.—The fact that so many gastric ulcers are latent, and the difficulty attending the diagnosis of simple cases has made it impossible to determine with accuracy the average duration. Many cases, if not the majority, are undoubtedly acute in onset, and while some heal rapidly within a few weeks or less, others are of many years' duration. In MacCallum's and Tull's cases, some had a history of ten or more years, with intermissions. It is difficult to say, however, how much of the history was attributable to ulcer, and in how many cases multiple ulcers occurring at long intervals may have given rise to the prolonged symptoms. Bolton holds with some justice that the destiny of an ulcer depends largely on its cause, and the adverse influences to which it is exposed; one may add on the possibility, too, of removing the cause.

The *mortality* from all kinds of ulcers is variously given as 8 to 10 per cent. (Riegel). Russel, in England, investigated the after-histories of cases of hemorrhage, and finds the direct mortality 2.1 per cent.; 4.3 per cent. died of intercurrent diseases; 42.6 per cent. recovered (27.7 per cent. had only one attack, and 14.9 per cent. recovered after one or more relapses); 6.4 per cent. were indefinite as to the prognosis and 44.7 per cent. still had gastric symptoms of varying intensity. Lenhartz's results seem to give a more favorable outlook, and modern surgery has improved the former unfavorable statistics. Relapses are frequent and may occur after several years. Einhorn draws attention to the fact that at post-mortems one sees twice as many scars as fresh ulcers. Sometimes a new ulcer forms alongside of an old and chronic one, and sometimes cancer forms on the ulcer and alters the outlook of the case. The contentions

of most writers as to "cures" must be accepted with some reserve—especially those with a high percentage of successes from the medical treatment of chronic cases, for the statistics most often proclaim a mere relief of symptoms rather than a permanent cure.

The course and prognosis are materially altered according as the physician can deal with the etiological factors, more especially with infective foci and sources of irritation. Removal of these renders the outlook more favorable, whereas chronic cases, in older people associated with progressive arteritis and other vascular lesions, are more obdurate. Traumatic ulcers are most favorable in their course if treated early and well.

Treatment. Methods of treatment of peptic ulcer have been, and still are, for the most part empirical, and hence in many ways unsatisfactory. Early statistics on ulcer therapy are useless and misleading. Our methods of diagnosis having been far from complete in former days, our "cures" were equally dubious. So-called "ulcers" frequently represented the irritating influences of extra-gastric conditions with disturbances of secretion and motility, all of which occur in many conditions other than ulcer, both in and outside of the stomach, but were frequently mistaken for ulcer and treated accordingly.

This has been amply demonstrated in the operating-room, where laparotomy for supposed ulcer has often ended by the removal of the appendix or draining of the gall-bladder. Older records, then, of the cure of gastric ulcer—both by medical and surgical means—must be warily received. Even surgically, the finding of the ulcer is not easy, and often the supposed ulcer is treated and "cured" by gastro-enterostomy without sufficient proof having been obtained of its existence! Hospital records of the medical treatment, too, have described a change in the severity of ulcer symptoms upon discharge which has been taken as a cure, whereas, after all, neither the underlying organic lesion was "cured" nor was a recurrence prevented.

The first essential in the treatment of gastric ulcer is a proper diagnosis: (1) Of the actual presence of ulcer. (2) Of its type with reference to the underlying anatomical condition, and whether or not it should be subjected to medical or surgical treatment. (3) Of the causes both immediate and remote. (4) Of the possibility of removal of the cause, whether this be some focus of infection, some toxic state, etc.

Medical Treatment. Primarily, ulcer is a matter for medical care, for surgical treatment does not eliminate the predisposition; in other words, the remote *causal* therapy is all important. While medical treatment relieves symptoms and often cures an ulcer, it is true that without a laparotomy, one is uncertain as to the coexistence of some infection in the appendix or gall-bladder, so that the mere cleaning up of an oral sepsis may still leave an abdominal focus untouched. Nor is it to be denied that recurrent attacks are liable to complications (hemorrhage, perforation and peritonitis), and further, that while the roentgen-rays may reveal a healed ulcer, it offers no assurance that there will be no recurrence.

The fact, however, that spontaneous healing of gastric ulcer is so common is sufficient justification for laying stress on purely medical treatment in all appropriate cases, and occurrence of so many failures can be

in large part attributed to insufficient care in the early stages of acute and subacute ulcers. Permanency of any established cure is likewise imperilled by laxity in the continuance of adequate medical therapeutic measures. It is especially suitable in the young, when the cases are early, as also in all other cases where coexisting serious disease elsewhere renders operative success improbable.

This care consists not alone in a suitable dietary, but in the essentials of personal hygiene, in educating the patient as to the proper rules for his treatment, in the removal of all etiological factors, and due consideration of pathological and physiological processes.

Under the category of "medical" cases come those which are acute or subacute, or even chronic, provided there is but little callus and if no obstruction exists. On the other hand, when there is extensive callus or where repeated hemorrhages have occurred, or the pain and other symptoms are persistent in spite of diet and medication, surgery is essential, *unless a positive Wassermann reaction is present.*

Rest is the first essential. In early ulcers, rest in bed is imperative (two to three weeks), and freedom from physical and mental effort. All authorities agree on the principle of rest, which was, after all, the original idea of Cruveilhier. Those who followed have emphasized this original idea of general rest to the body and local rest to the stomach, and particularly to the ulcer. It is chiefly in respect of what best affords this rest that the authorities differ. What, after all, does constitute rest to the stomach and the ulcer? Does complete starvation really give rest to the secretions and muscle of the stomach or is more achieved by the administration of small quantities of food? Does the administration of food unnecessary promote secretions and peristalsis? Is it wise to withhold carbohydrates or proteins or fats? Do alkalies contribute to rest or do they not? Are such drugs as bismuth, opium, etc., really beneficial? All these questions, despite the observations of years, still await definite answers. We are still in the realm of theory as to the actual conditions which underlie these various treatments.

Lenhartz, for example, urges excess of proteins in the diet to counteract the hypersecretion that occurs. Sippy, on the other hand, commended the use of frequent feedings and alkaline treatment, which others claim will overstimulate both secretion and motility. Smithies recommends oral starvation at first and uses later a carbohydrate diet with vegetable proteins, and disapproves of alkalies. Coleman objecting to all these forms of diet for peptic ulcer, claims that the only rest for the stomach is that supplied by a diet of fats. With these differences on the part of experts it is difficult to determine wherein exists a perfect remedy.

Certain *general rules* of diet may be laid down for acute cases. For the first few days, provided no hemorrhage has occurred, the patient may take small amounts of milk and cream, gruel or albumin water (2 to 4 oz.) every two to three hours, giving in the interval small doses of alkaline powders to neutralize a possible hypersecretion. Then cooked cereals, alternating with the milk and cream, or with soft-boiled eggs may follow. This diet may be gradually increased in quantity and olive oil in doses of 2 to 3 oz. may be given three times a day with the alkaline powders. In

two to three weeks, custard, junket, light puddings, small quantities of stale bread and butter and cream cheese may be added. During the first month, no more solid food should be administered, and when these are commenced, they should be prepared in finely-divided form, given in small amounts, be well chewed, and milk and cream given in between these light meals. *Pain*, which is primarily due to peristalsis acting on an irritable focus, is best relieved by neutralizing or suppressing the acidity, which in turn inhibits the peristalsis.

Smithies holds that absolute rest to the ulcer is attained only when less peristalsis and less spasm are obtained. This comes from the avoidance of any food, lavage or medication by mouth. The patient is thus starved from three to seven days, being given only 15 cc. of warm water every hour, and occasionally some sips of orange juice or grape-fruit juice. The patient is encouraged to chew paraffin wax to stimulate saliva and provide a protection to the mucosa. Rectal feedings (four to six daily) are given by the drop method, the solution used being: 50 per cent. alcohol, 30 cc.; glucose, 30 cc. and normal salt solution to 240 cc. When feeding begins, it must be liquid, warm, in small amounts, and consist of carbohydrates only. Such food leaves the stomach quickly, there is less tonus, less activity, less distention and less secretion of gastric juice. He recommends gruels of rice, wheat or barley, thin purées of vegetables, and malted milk. Each feeding must be not more than 4 to 6 oz. After some days, he adds custards, buttermilk, purées of eggs, and, later, steak in addition. He disapproves of the use of alkalies because physiological increase of acid secretion occurs and often demands aspiration. He believes that the diet above recommended affords relief from the symptoms *without* the use of alkalies.

Spasm is usually relieved by the rest and diet alone, but if the ulcer be near the pyloric orifice, anti-spasmodics (atropine) may be required. If the gastric irritability is unusual, or if the patient demands food, one may use duodenal alimentation with liquid carbohydrates, as recommended by Einhorn. Local applications over the abdomen of hot alcohol and boric acid, kept warm by an electric pad, are recommended. Etiological therapy is strongly advocated. Septic foci must be removed, whether in adenoids, tonsils, teeth, appendix, gall-bladder, ears or nasal sinuses. The Wassermann test is naturally required. If anemia be marked and persistent, whole blood transfusion is urged.

Suggested objections to these treatments refer to the fact that raw fruit juices are too acid for any such condition as acute ulcer; that the carbohydrates used have too much protein, and are, therefore, food mixtures, not pure carbohydrates; the ingestion of such foods prolongs the digestion, and adds to the secretion, even more than does meat; that too frequent feedings prevent rest to the stomach and both secretion and motility are maintained.

Sippy urged rest, and the patient, if need be, may remain in bed for several weeks. Food is given every hour during the day; the first feeding consists of 3 oz. of cream and milk, equal parts, and later on, soft eggs and cooked cereals are added or given alternately. Six ounces is the maximum for one feeding. After a few days, cream soups, bread and butter

and soft foods are added. The acid is controlled with alkalies given between each feeding, and the following powders are used alternately. Calcined magnesia powder, and sodium bicarbonate āā. gr. 10 (0.6 gm.) The other powder consists of: Calcium carbonate, gr. 10 (0.6 gm.) and sodium bicarbonate, gr. 30 (2.0 gm). These are given in 2 oz. of water. After the last feeding at night, four more powders are given, one every half hour or until the stomach is presumably empty. Sippy recommended aspiration of the stomach two hours after the last feeding to ensure it being empty and to lessen night secretion. If the need should arise, more sodium bicarbonate can be given to control the acidity and occasional lavage employed.

After several weeks, light meals are given, but the cream and milk are continued every hour. When the hourly feedings are stopped, the powders are given for three hours after meals. The only medicines recommended are atropine and opium, atropine for the excessive secretion and opium as required for the pain. Saline injections or enemata are given as required.

The features of this treatment are frequent feedings and much fat in the diet and there is no doubt that a constant demand is made upon the activity of the stomach. While experience teaches that this treatment undoubtedly gives relief to the symptoms, it does not seem easy to be sure of cures, nor is it easy to believe that chronic callous ulcers are curable by methods such as these. Secretion is probably diminished because of the excess of fat in the diet. The HCl is neutralized by the alkalies but constant motor activity is inevitable and it is doubtful if much digestion takes place until the food reaches the duodenum.

Hardt and Rivers sound a note of warning with reference to the toxic symptoms that may result from alkaline treatment. In 16 of their cases, toxic symptoms developed. There was marked increase in the blood-urea and creatinine. The CO_2 varied in the normals from 55 to 70 vols. per cent., and in the toxic cases from 65 to 117. During toxicity, the average total acidity was 78, and the free HCl. 48. The symptoms arising were: Headache, nervousness, introspection, nausea, vomiting, joint and muscular pains, weakness, slow respiration and rapid pulse, flushing of the face and sweating. Upon discontinuance of the alkaline treatment, the symptoms disappeared.

Coleman's method has for its general principle secretory and motor rest to the stomach and sufficient nourishment for the patient. He endeavors to select foods which excite least secretion and motor activity, and therefore chooses fats. He insists on pure fats not mixed with other foodstuffs. For carbohydrates he uses glucose per rectum; none is given by the mouth. Enemas of glucose—30 grams in 300 cc. of physiological sodium chloride solution—given hot by the drop method, are recommended four times daily throughout the day. If cramps should occur, the amount or number of times should be reduced. No food is taken until the third or fifth day, but if the patient is thirsty, a little water may be given. Egg white follows, and olive oil or butter, fresh and unsalted. These two are given alternately every two hours, and the allowance is increased according to circumstances. The total amount of feeding is never over 3 oz. The amount of olive oil (chilled) may vary

from 1½ to 2 oz. on the first day: egg white 3 to 4 oz., thoroughly mixed with water. The oil is increased to a maximum of 150 cc. per day, with 6 or 8 eggs. One may substitute egg yolk for oil or butter. If the patient is rebellious over this form of fat, cream may be given instead (690 cc. of cream are equivalent to 150 cc. of olive oil). This treatment continues for two or three weeks, after which specially selected foods are given for some months. Coleman holds that this method affords an ideal means of rest to the stomach, giving ample nourishment and a fair amount of comfort.

Einhorn devised a method of feeding directly into the duodenum by a duodenal tube and claims success in suitable cases—with persistent bleeding and tendency to stasis. The method does not seem to have received general approval, though in theory much might be said for it.

Ambulatory Treatment.—Truman and, later, Rehfuss, have suggested special diets for ambulatory cases. The former recommends rice water feedings for one or two hours, with milk and cream in combination, and in between the treatments, calcium carbonate sodium bicarbonate, and magnesium oxide. The rice water mixture is given as a substitute. The formula is as follows:

Boil ½ cup rice in 5 cups slightly salted water until soft.

Strain and cool.

Add 4 tablespoonfuls lactose, whites of 4 eggs, slightly beaten, ½ cup cream.

One quart of this, which equals 750 calories, may be made palatable with coffee, peppermint or chocolate.

Rehfuss insists that the successful medical treatment depends on its duration, and careful dieting should be carried on for several months (six). It is essential, however, first of all to remove foci of infection.

When hemorrhages have occurred, the patient should remain in bed two weeks, as also after a hypersecretory crisis, when a rigid diet and lavage should be used, with peptonized milk and neutralizing powders.

For medication, he recommends: Strontium bromide, gr. 10 (0.6 gm.), tincture belladonna, m. 5 (0.3 cc.) before the three main meals, and neutralizing powders one hour after meals.

Surgical Treatment.—It is futile to discuss the comparative values of medical and surgical treatment. Each method deals with different types and our present means of diagnosis have, to some extent, simplified the matter of choice in therapy. Medical treatment is always to be used in early cases without deformity, perforation or recurrent hemorrhages, and when there is no marked cicatrix or obstruction. In these cases, our chief guide for diagnosis and prognosis is radiological. Chronic cases, on the other hand, with deformity, obstruction, much calloused ulcers or recurrent hemorrhages—even oozings—all necessitate early surgical consideration, and it is but a waste of time to attempt medical therapeutics. Medical care is, nevertheless, essential prior to and subsequent to all operations, and is of prime importance in effecting a permanent cure.

Bastedo is a stronger advocate for medical treatment than most of his contemporaries, and discusses chiefly the excessive use of gastro-enteros-

tomy on account of its mortality of 3 to 6 per cent. and subsequent jejunal ulcers in 2 to 5 per cent., as well as the fact that often it does not cure, nor does it stop cancer, hemorrhage, perforation, or new ulcers. In view of these dangers, he urges more careful medical care prior to surgical interference. Krohn, following for ten years 266 patients treated medically, obtained records of 172 cases. The duration of the ulcer, he found, did not much affect the prognosis, though it is better in younger than in older cases. In those over forty years, 48 per cent. did well; in those under forty years of age, 75 per cent. were notably improved. Of the 172, 11 men and 23 women died; 10 of these from gastric hemorrhage. Only 3 of the 172 developed cancer and 1 died of perforation. All other deaths were from extra-gastric causes.

Results of Operations.—*Treatment of Hemorrhage.*—Finsterer holds that 21 per cent. of all open ulcers die of hemorrhage. In only one of 91 cases of hemorrhagic ulcer was mere erosion present. In 51 operative cases, the mortality was better than where medical treatment alone had been employed. In Clairmont's cases, the mortality was 26 per cent. Finsterer's surgical mortality was 19 per cent. He recommends early operation before exsanguination takes place. In these cases gastro-enterostomy is useless; resection alone is profitable.

As a general rule, operation soon after a hemorrhage should be avoided. Fifty per cent. of those operated upon immediately after hemorrhage died, while, on the other hand, a resection done during the later anemic period, is usually curative. Emergency operations for gastric hemorrhage are always dangerous, and most authorities insist that gastro-enterostomy for these cases is apt to lead to fatal results. Where the large vessels are apparently eroded, transfusion is imperative, and narcotics should be avoided.

Surgical Methods and Indications.—Duval and Moutier distinguished 2 types of *perforation:* (1) Where the lesion is chronic, aseptic, with the rupture as a mechanical accident. Here simple suture and gastro-enterostomy suffice. (2) Where the perforation is the result of an infection with suppuration and necrosis. Here wide resection is more urgent. They regard this distinction as accountable for differences of opinion as to the nature of treatment. Howard states that 8 cases have been recorded as recovering after generalized peritonitis without operation, and Carless' statistics, which likewise seem optimistic, give 4 per cent. recovering under similar conditions. The early surgical treatment as a result of prompt diagnosis and perfected technique has given brilliant results, and statistics afford ample evidence of the success of more modern methods. Gibson reported on 60 cases of perforation, illustrating the value of early treatment, and confirming his belief in the importance of simple closure of the perforation without further procedure. The mortality in his total series was 16.6 per cent. In 43 cases operated on within twelve hours, the mortality was 6.6 per cent.; in 5 cases within twenty-four hours, there was 1 death, while in 10 operated on after twenty-four hours, there were 6 deaths, a mortality ratio of 60 per cent. In 56 of Gibson's cases, where suturing alone was done, there were 9 deaths. J. Bell, of Montreal, as early as 1903, had 10 cases, with no deaths. The

proportion of recoveries has a direct relation to the early time of operation after rupture; the sooner operation is done, the greater proportion of recoveries.

The multiplicity of ulcers is of the greatest importance, and is to be considered in all operations for perforation, and in not a few cases a second operation has been necessary for this reason, when the first had healed. Hence the recommendation of some surgeons to perform a gastro-enterostomy in all cases after closing the perforation, in this way obviating possible extension of other ulcers.

Hour-glass Contraction.—The treatment of this is essentially operative, the object being first to drain both sacs and allow of healing, which, however, involves a double operation. Many methods are recommended. (1) Gastroplasty, which affords better communication between the two sacs, is a suitable operation for the simpler cases with little infiltration. It is done with or without gastro-enterostomy, according to the requirements. (2) Gastro-gastrostomy, in which the two sacs are brought together and directly joined, is often commendable in patients whose hour-glass contraction is extreme, and where the opening between the sacs is very small. (3) Partial gastrectomy, which removes the total area of disease and unites the divided healthy ends of the stomach, is the ideal operation, because it corrects the deformity as well as eliminates all the old or any recent disease. (4) Gastro-enterostomy alone is of little use. To be beneficial it should be double—a serious operation with some danger of a double vicious circle. The necessity for anastomosis is largely determined by the situation of the ulcer, its extent, and its liability to induce stenosis, adhesions and deformities.

DUODENAL ULCER

From a surgical standpoint, the pyloric vein divides the stomach from the duodenum. To the physician, however, this exact boundary is not always clinically satisfactory. The symptoms and signs may be those of gastric ulcer in many instances where the lesion is found beyond the pyloric vein, and, *vice versa*, pyloric lesions may give every clinical evidence of being duodenal ulcers. Nevertheless, there are many duodenal ulcers which occur in the bulb with definite characteristics and to these special reference should be made.

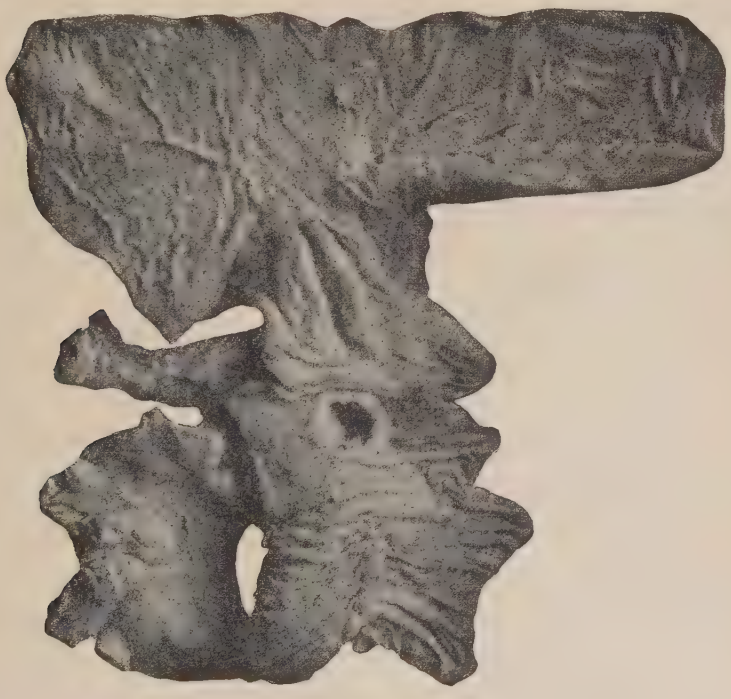
Duodenal ulcers are much more common than was previously supposed. In the Mayo Clinic, over a recent period of fourteen years, there were 4 duodenal ulcers to 1 gastric; and Moynihan found more than 2 duodenal ulcers to 1 in the stomach. Rosving, and also Sherren, found about equal numbers of duodenal and gastric ulcers in their experience. Acute and chronic ulcers are found in the duodenum as in the stomach, and the acute are almost invariably of infectious origin, more especially from a chronic appendicitis.

Sex.—These ulcers are more frequent in males (149 to 27 females). In Choyce's series (1920) 80 per cent. were males. He accounts for this predilection by the greater frequency of appendicitis in males, and more gastric hypertonicity.

Age.—The are most frequent in the third and fourth decades but may be found at any age. H. P. Wright, of Montreal, mentions 100 cases on record in infancy. Perforation is recorded in an infant of twenty-one hours, and hemorrhage from a duodenal ulcer caused death in another infant only two days old. The chronic cases are essentially in adult life.

Pathogenesis.—For the most part, the duodenal ulcer has a similar origin to gastric ulcer. Infection undoubtedly plays a very important part. T. Gray is of the opinion, however, that the pathogenesis differs in duodenal ulcer from that of gastric ulcer. The relative increase in vagus excitation is established by diminished sympathetic control, or by

FIG. 35



Duodenal ulcer.

increased vagus stimulus, and this constitutes a predisposing factor in the development of duodenal ulcer. In other words, there is excessive motor and secretory activity. Hurst regards duodenal ulcers as an accompaniment of hypertonic gastric states, while gastric ulcers occur with hypotonia. One may say in general that any nutritive injury to the duodenal mucosa from whatever cause, vascular, nervous or infectious, makes possible a digestion of tissue, and thereby gives rise to ulcer.

Matier associates 90 per cent. of adult cases with tobacco. It has long been known that severe burns at times precede duodenal ulcers by one or two weeks. Toxemia resulting from such lesions may cause erosions which later develop into true ulcers. Reeves points to the vascular arrangement

of the duodenum and to the anemic "spot" in the first portion of the duodenum, an area more vulnerable than other parts of the viscus. Judd distinguishes two types: (1) Simple; (2) ulcer with duodenitis but no crater. Clinically, there is but little difference.

Number.—These ulcers are usually single (80 per cent.); Collins found two ulcers present in 11 per cent. of his cases and more in 4 per cent. When multiple, these ulcers are usually crowded together in the first portion. In contrast to the gastric ulcer, they are usually uniform in size and appearance.

Site.—The site is usually on the posterior wall, and suprapapillary. Ninety per cent. occur in the first portion and extend to within one-half inch of the pyloric centre. The deepest portion is just below the pylorus, where the acid chyme most affects the intestinal mucous membrane. They are much more rarely found on the anterior wall and only very occasionally in the descending portion.

Symptoms.—Not infrequently, these ulcers are *latent*, and there is little doubt that the healing of a duodenal ulcer is not so rare as Melchior thought. Kratzin and Gruber found 18 duodenal ulcers with scars and 43 not healed at autopsy. Stewart found half as many scars as ulcers. In a large number of cases, the symptoms are often typical of the seat of origin, and the history is all important in the diagnosis. As a rule, the duration has been for many years.

Pain, which is the chief symptom, is usually more delayed after meals than in gastric ulcer, and continues on to the next meal, *i. e.*, it does not coincide with digestive peristalsis. It is not infrequently referred to the breast, back or shoulder, and in its acute severity reminds one at times of biliary colic. It occurs regularly day after day, and frequently between the hours of two and three in the morning. It is often relieved by food, especially solid food, and by albuminous drinks, also by lavage or alkalies. *Periodicity* is marked and the intervals between the attacks are much longer than in gastric ulcer. The attacks themselves are often from three to four weeks' duration, while the intervals of health may last for months. The symptoms are often precipitated by cold, fatigue, worry and dietetic indiscretions. *Vomiting* is much less common than in gastric ulcer; it is irregular, delayed, often acid, and the amount varies according to the degree of obstruction or hypersecretion. *Hypersecretion* is a very frequent accompaniment with the train of symptoms dependent upon it. The appetite remains good and constipation is the rule.

Icterus occurs in 13 per cent. of the cases, due, perhaps, to scarring of the ulcer in the second portion of the duodenum or involvement of the common duct or pancreas in the inflammatory process. *Hemorrhage* from duodenal ulcers may be small and recurrent, or may be short and large, and cause fainting, collapse, and even death. The diagnosis is made frequently from the association of the symptom-complex combined with repeated evidence of melena. Sometimes hematemesis and melena occur together, and in about one-third of the cases, the intestinal hemorrhage is obvious to the naked eye. It is hard to check and usually of longer duration than in gastric ulcer. *Tenderness* varies very much. It should be noted that Rosving disputes reliance upon the so-called

symptom-complex as being pathognomonic; in fact, a similar train of symptoms occurs, he maintains, in ptosis, gastric ulcer and gastritis.

Physical Examination.—While it may be true that the symptom-complex is all important in the diagnosis, it is none the less essential to make a very complete examination, both to exclude other possible maladies and to make a definite decision. The abdomen at times presents a rigid rectus on the right side, and there may be tenderness in the epigastrium on deep palpation.

Roentgen-rays.—By means of the fluorescent screen, one often sees in acute ulcer early hyperperistalsis, and later, hypoperistalsis, with deformity in the bulb. Palpation under the screen of the tender point is an important adjunct in the diagnosis. Deformities in chronic duodenal ulcers are often best demonstrated by changes in the bulb, where 95 per cent. of duodenal ulcers occur. Normally, the bulb shows a round, convex, linear, circumscribing line of bulb shadow in pear or chestnut shape. There is a normal diffused density of shadow and a stability of filling. With duodenal ulcer, there is a definite deformity, with changes in the edge, with indentation (niche) or projection; sometimes hour-glass forms or clover-leaf forms are found. There is retraction of the bulb, with flattening in the longitudinal direction. The canal of the pylorus is often lengthened, while the antrum is continued into a fine, thin, shadow, to which the bulb shadow is attached like a cherry on a stem (Haudek). The bulb shadow itself shows less density and the filling of the bulb is more transitory because of the hypertonus of the muscle of the stomach and duodenum.

Recent cases of duodenal ulcer show hypertonia of the lower half of the stomach, and sometimes a pressure pain over the bulb. The stomach empties rapidly, whereas the bulb may fill well and show a persistent shadow. The picture of the older and more chronic cases is different and shows both by direct and indirect means evidences of ulceration, but there is apt to be retention of food in the stomach and characteristic deformities in the bulb.

The objective evidences by physical and chemical examinations have a varying value and rarely show much that is pathognomonic, and the chief reliance, apart from the history, rests upon the roentgen-rays.

Complications.—These are numerous, and the most notable are: Perforation, periduodenitis, and deep penetration into the retro-peritoneal tissue with subsequent phlegmon. Exceptionally the liver is penetrated. Implication of the surrounding viscera and organs is not uncommon, or there may be involvement of the gall-bladder, bile ducts, pancreas, etc. There may be cicatricial stenosis of the duodenum and ampulla of Vater, with obstruction of the outflow of bile and pancreatic juice, compression of the portal vein, and cancer. Perforation of duodenal ulcers present much severer symptoms, according to some authors, than do gastric ulcers, but the mortality after operation is about one-half.

Diagnosis.—Wrong diagnoses are frequently made, and many cases with perforation have been mistaken for appendicitis (19 out of 51, Moynihan). Early operation is most important and delay beyond twenty-four hours adds greatly to the risk.

Perforation.—Perforation is not infrequent and in most instances occurs on the anterior surface. Of 131 cases, 91 per cent. were in the first portion, 6 per cent. in the second portion and 3 per cent. in the third portion. Twenty per cent. of all cases occur without previous warning; in others, the average duration of symptoms is about four years. The favored treatment is by closure alone, though many authorities agree that when the patient's condition warrants it, a gastro-enterostomy should also be done. The operative mortality is about 10 per cent., varying with the time after perforation has occurred. In Gibson's series of 32 duodenal perforations, there were 4 deaths.

Prognosis.—The course is often of very long duration, always with a possibility of dangerous complications, especially of perforation.

Treatment.—In typical duodenal ulcer this differs in one respect from that of gastric ulcer. Medical care apparently merits more consideration, and surgeons are not always so enthusiastic regarding operation as in chronic gastric ulcer. Forsythe gives an interesting comparison between the medical and surgical treatment of duodenal ulcer. The statistics are taken from the Medical Sickness Annuity Society. There were 59 cases and 119 claims with 22 relapses. Surgical treatment had been undertaken in 56 per cent. and medical treatment in the remainder. There seemed very little difference in the length of time required for restoration to complete health; if anything, the records for surgical cases were more protracted. The same holds true of the permanency of the cure. Three operative cases died but there was no record of death among those treated medically. It would seem from the reports that the majority of patients recovered after one attack and remained free, while the minority last over a period of several years.

Duodenal alimentation is apparently worthy of trial at times. Friedenwald and Geist found it neither difficult nor uncomfortable, and applied it more particularly when vomiting and nausea occurred and when feeding was difficult in post-operative cases. Others regard the duodenal tube as a foreign body and a source of irritation.

In every case of duodenal ulcer, medical treatment should be attempted prior to operation. The treatment must be thorough or justice is not done to the patient. The patient should be placed in bed, and have complete rest for two weeks. Rest should be given to the stomach as in gastric ulcer, and patients should be given a diet consisting of milk mixed with some cereal for the first few days without further food. Water should be given by the bowel to alleviate the thirst. After a few days of such treatment, other soft and non-irritating foods may be given, care being taken chiefly to avoid acids, sweet and fried foods. Frequent feedings must be given, and such a regimen should be maintained for months.

The use of *alkalies* in duodenal ulcer has been much discussed, and there is no doubt that, under certain conditions, danger attends their generous use. Antispasmodics are of more benefit than alkalies, and should be given freely during the period of attack.

Indications for surgical treatment may be outlined as follows: (1) Chronic callous ulcers with stenosis; (2) periduodenitis causing deformities; (3) perforation; (4) recurrent attacks with copious repeated hemor-

rhages; (5) chronic cases with repeated small hemorrhages which fail to heal after a thorough medical treatment of six to eight weeks.

Gastrojejunostomy alone is quite satisfactory in free ulcers (if definitely found!) and where mechanical considerations are taken into account. Foci of infection must always be removed from every source. Excision is indicated only where it appears easy to do and where the duodenal lumen can be well maintained; it is applicable to the bleeding type and when much and persistent local pain exists. Ninety per cent. are cured (Moynihan).

Haggard and Floyd have recorded the surgical results. In 100 cases operated on, there were 78 with gastro-enterostomy (short-loop retro-colic implantation type) at the most dependent part of the stomach. Of these 60 were traced, and 80 per cent. of them reported as cured. They believe that a well-placed and well-executed gastro-enterostomy in duodenal ulcer is gratifying in its results in the average case. Finsterer, in 225 cases, had a mortality of 4.8 per cent. He insists on the importance of resection of the ulcer, with gastro-enterostomy, which treatment, when successful, gives 93 per cent. of cures. Other records show that gastro-jejunostomy has comparatively few failures, and a high proportion of cures. The operative mortality rate is low (0.5 to 1 per cent.) and less than 2 per cent. of operations are failures.

CANCER OF THE STOMACH

Definition.—A malignant epithelial neoplasm of the stomach.

Incidence.—About one-half of all cancers arise in the stomach, and statistics of hospital *admissions* show 0.47 per cent. of gastric cancers. *Autopsy* statistics show 4 per cent.; Reiche's Hamburg statistics (1872 to 1895) show that 50.2 per cent. of all cancers are gastric.

Regional.—Deaths per 1000 population from cancer in general vary within wide limits; Amsterdam, 12; Berlin, 22.4; Geneva, 53; New York, 19.3; and London, 28.7. Climatic conditions have but little influence except that in tropical countries gastric cancer is more uncommon. Regional differences are probably associated more with the manner of living and the diet than with the climate.

Etiology.—Race.—Gastric cancer is much less common in negroes. In 1880 the death rate in the United States from all cancers was: white, 25.9; negroes, 12.6.

Age.—The following results appear from 7000 collected cases.

Ages.	Per cent.
10 to 20 years	0.08
20 to 30 years	1.5
30 to 40 years	8.4
40 to 50 years	18.0
50 to 60 years	28.0
60 to 70 years	28.0
70 to 80 years	14.0
Over 80 years	2.0

Congenital cases have been described (Williamson and Widerhofer), and Cullingworth performed an autopsy on a child, aged five weeks, in

which gastric cancer was found. Osler and McCrae found 10 cases in the literature under ten years of age, and 13 cases between ten and twenty years. Probably more than 2 per cent. of all gastric cancers occur under thirty years of age; 80 per cent. or more between the ages of forty and seventy. With better methods of examination more and more cases are found among youths, which alters the ratio somewhat and brings the average down to earlier years.

Sex. Of 20,000 cases collected from our combined statistics, 58 per cent. were in men. Welch gives the relation as five males to four females.

Heredity.—Opinions vary widely and statistics are very incomplete. In 1075 cases Snow found heredity in 167, *i. e.*, 15.5 per cent.; Schule gives 6.5 per cent. as hereditary; Lebert 7 per cent., and Roth 50 per cent. Of 2700 cases of gastric cancers, 12 per cent. showed an hereditary history. In the Royal Victoria Hospital, 24 per cent. gave a probable hereditary history, which was undoubted in 18 per cent. Cancer as a family affection perhaps occurs in 10 per cent. in all cases. Since gastric cancer is common, there can be little that is reliable in such findings.

Previous Gastric Disease.—Long-continued irritation as a cause of cancer of the stomach is extremely dubious, and "badly used" stomachs seem to suffer no more than do those well treated. On the contrary, the development of cancer is often almost sudden when the digestion had previously been unimpaired.

Chronic Ulcer and Cancer.—Wide variations in the statistics are noted, because of many views and imperfect observations as to the diagnosis of ulcer. Cruveilhier discussed the relation of cancer and ulcer in 1839, and Rokitansky soon after recognized its possible implantation in ulcer. Dittrich, in 1848, recorded 160 cases of cancer, of which 6 were of this etiology. Fütterer concluded that cancer frequently formed at the edge of ulcers, especially where the part was most exposed to irritation, and in the pyloric region this development occurs in the lower margin. But if the position of the organ alters from dilatation or adhesions, other parts of the edges may be involved. Cancer develops in ulcer most frequently in the pylorus. (Fuller discussion of the subject will be found in the article on gastric ulcer.)

Alcohol.—Fifty-six per cent. of the Royal Victoria Hospital cases were habitués, and of these 20 per cent. were hard drinkers, and 30 per cent. drank moderately but constantly.

Trauma.—In 62 cases of cancer of the intestinal tract, Boas found 9 with a clear history of antecedent trauma, and *only* 1 *in gastric carcinoma*. According to some, trauma has a definite effect in aiding the development of latent cancers and increasing the rapidity of their progress. Trauma, as applying to irritation of various kinds, may be considered a factor.

Auto-inoculation.—Transplantation of cancer from a primary growth on the tongue into the stomach has been recorded by Klebs, Cornil, and others, but such instances must be very rare. The possibility of auto-inoculation from one cancerous tissue to another has been frequently noted, and surgeons have found it in the line of incision or of puncture in abdominal cancers infected from the original neoplasm.

Pathology.—Cancer of the stomach is a malignant epithelial overgrowth extending from the secreting cells of the mucosa to the other coats of the organ, and thence usually to the neighboring tissues, glands, and organs, or to distant parts by continuity, contiguity, and metastases through lymphatic and blood channels.

Secondary cancer of the stomach is rare. Statistics show the proportion to be about 1.1 per cent. (*i. e.*, 5 cases out of 440), up to as high as 6 to 7 per cent. (Hale White). It arises either from contiguity or by metastases from distant viscera. Involvement by contiguity from the pancreas, liver, œsophagus, etc., is, of course, common and even transplantation from the tongue has been recorded.

Site of Growth.—The pylorus (27.2 per cent.) and the lesser curvature (26 per cent.) are the most frequent sites. The frequency of the latter site accounts for the absence of obstructive signs in many cases of apparent pyloric cancer in which the *x*-rays show the patency of the pylorus. Mikulicz and Kausch, in 1900, mentioned the probability that 40 per cent. of cases of cancer of the stomach began in the lesser curvature, their observations depending on laparotomies and thus representing earlier types than are seen by the pathologist. As regards other sites of origin, two series may be quoted:

	Pylorus and lesser curvature. Per cent.	Cardia. Per cent.	Diffuse. Per cent.	Anterior or posterior wall. Per cent.	Greater curvature. Per cent.
Lebert and Hahn.	51	29	15	0.08	0.04
Orth	80	10	10		

Multiple Cancers.—Occasionally several tumors are found, *e. g.*, Maurizio saw one case with cancer at both the pylorus and cardiac end, and Gierke reported a case with four cancers in one stomach.

Relation of Cancer to the Changes in the Mucosa.—The general mucosa elsewhere suffers coincidently with the progress of the cancer. Usually the superficial cells are fairly preserved or more goblet cells appear. The peptic glands become mucous glands, the border cells disappear more than the chief ones, and all are more or less surrounded by new small round cells. The mucous membranes may be completely absent in some places, due to the development of a general atrophic gastritis with small-celled infiltration, cysts, etc. The observation of Fenwick is noteworthy, viz., that with cancers of organs other than the stomach there may be absence of normal acid gastric juice. Friedenwald and Rosenthal found a similar result in 9 out of 29 patients.

The cancer may be circumscribed or diffuse, *i. e.*, a fungating mass with a villous surface, or one that is more smooth and flat, and showing central dimples or areas of degeneration and ulceration, or else diffuse, extending mainly in the submucosa, which thus becomes thickened, giving to the whole wall a greater rigidity and firmness. The mucous membrane itself is usually roughened and in parts degenerated, while the organ is either large and dilated (if pyloric stenosis has occurred), or shrunken and the cavity much smaller than normal. In some of these diffuse cancers it may be impossible to distinguish the condition from a mere cirrhosis (interstitial gastritis) even by microscopic examination.

Two main types occur: The *scirrhus* and the *medullary*, although transition forms and mixed types are usually present in nearly all gastric cancers. Duggan's statistics record 56 per cent. of adenocarcinoma, 20 per cent. of scirrhus, 8 per cent. of colloid and 16 per cent. not specified. The mixed types are, as a rule, hard tumors, due to the preponderance of fibrous tissue (where epithelium and stroma preserve the alveolar arrangement the name *carcinoma simplex* is used). The wall is thickened, the extension is often diffuse rather than circumscribed, and there is a tendency to scar formation in some places, while in others superficial ulceration is seen. Scirrhus cancers are slow growing, spread gradually into the surrounding tissues, especially the muscle. It is in this form that differentiation is sometimes difficult between cancer and simple chronic

FIG. 36

Scirrhus carcinoma of pyloric end of stomach.

indurated ulcer or cirrhosis ventriculi. Many authorities regard *linitis plastica* as merely a cellular form of scirrhus cancer. Scirrhus neoplasms are commonest at the pylorus, so that stenosis occurs, owing to the increasing size of the tumor or to shrinking and rigidity at the orifice.

The *medullary form* is soft, very cellular, and thus on section shows more "juice." The progress is more rapid, degeneration and hemorrhage more common, and metastases are more readily formed. The glands especially are subject to invasion.

Papillary outgrowths of a special *adeno-carcinomatous* form are not uncommon. They form soft, fungating excrescences, oftenest at the pylorus, where they are sharply delimited at the duodenal end. Ulceration, necrosis, hemorrhage, and even perforation are apt to occur.

The *colloid changes* may supervene in any form of gastric cancer.

Diffuse thickening occurs from the presence of yellowish-brown, jelly-like, translucent fluid, which is seen occupying large or small spaces in the neoplasm. It is essentially a degenerative process of the cells and tends to invade the omentum, but not, as a rule, the intestines.

Myxomatous degeneration may occur in the fibrous stroma of any cancerous tumor.

Squamous-celled cancer commonly occurs about the cardia as the result of an epithelioma commencing in the œsophagus. It is rarely elsewhere in the stomach, except when secondary nodules form there either by transplantation from squamous-celled tissues (tongue, œsophagus), or by metastases from the œsophagus.

Extension and Dissemination.—The disease may be confined to the stomach, and may induce ulceration, degenerative changes, hemorrhages, etc. Extension within the stomach occurs chiefly by the lymphatics which run in the fibrous intersections between the muscle bundles. Here the course is vertical toward the serosa, which may also be involved. Cuneo has shown that the gastric lymphatics run toward the glands along the lesser and greater curvatures, more especially toward the pyloric end and in the adjoining portions of the great omentum, and thence through the cœliac glands on their way to the thoracic duct, thence to the supraclavicular region, as well as to the subclavian vein and the general circulation. In pyloric cancer the lesser curvature is rapidly invaded, and the lymphatics and glands become involved as far as the point where the coronary artery joins the stomach; here the lymphatics pass *from* the lesser curvature. The lymph nodes of the greater curvature do not usually go farther to the left than a point near the median line. The fundus is almost devoid of lymphatics.

The disease commonly spreads in the subserosa and if degeneration occurs here, ulceration, and even *perforation* may follow with a consecutive peritonitis, general or local with adhesions, and perigastritis. Perforation is, however, an uncommon event (4.46 per cent.), though perhaps more common than is realized. A perforation of an ulcer on the anterior wall or greater curvature should arouse suspicion as to its cancerous nature. In this way abnormal communications may form between the stomach and other viscera and tissues, *e. g.*, large intestine (gastrocolic fistula), small intestines, the anterior wall, pleura, pericardium, with admission of air and infected material into these cavities, the lungs and bronchi, with formation of abscesses, gangrene, etc.

Sometimes there is *partial healing;* scars form, although the process does not cease, and in other parts the neoplasm shows progressive degeneration. *Ulceration* occurs in a very large number of cases, probably in more than 80 per cent., and hemorrhages are common, the amount depending on the size of the eroded vessel or the degree of capillary oozing. Suppuration occurred in 4 of 40 cases observed by Boas.

Extension *outside* of the stomach occurs through continuity of structure, contiguity by adhesions, or by direct implantation, chiefly by the lymphatics and sometimes by the blood stream, especially the portal vein.

Metastases arise either from the blood stream or lymphatics. They may appear before any suspicion is aroused of the gastric origin of the

neoplasm, as in Tilling's case in which a secondary node on the humerus was the first evidence of the gastric cancer. Often, too, the growths in the liver or peritoneum mask the original site. Metastases travelling by the *blood stream* most commonly enter the portal vein and liver. They also commonly extend to the peritoneum and omentum, the pancreas, spleen, kidneys, pelvis, bones, and lungs (especially the left). No organ is immune. The *lymphatics* bring metastases to the neighboring glands (85 per cent., according to Cuneo), chiefly those at the diaphragm, the perigastric and retroperitoneal glands, the extension occurring in the glands of the thorax and *supraclavicular* region as well as in the thoracic duct. Out of 556 cases the cervical glands were involved in only 21 (4 per cent.). Statistics show that in 2156 cases, metastases formed according to the following proportions in various parts of the body: glands, 44.1 per cent.; liver, 33.2 per cent.; peritoneum and intestine, 27.6 per cent.; pleura and lung, 7.3 per cent.; and pancreas, 7.6 per cent. In the Tübingen statistics (1891 to 1905) the distant glands were involved only in 7 out of 91 cases; in only 3 were the supraclavicular glands involved, and in the others the bronchial and mediastinal glands. Cancer of the cardia often extends to the œsophagus; that of the pylorus, on the other hand, rarely involves the duodenum.

The *abdominal wall* is at times invaded, chiefly through lymphatics of the obliterated umbilical cord, and great diagnostic importance attaches to the discovery of small secondary nodules in the subcutaneous abdominal tissue, especially about the umbilicus. Peritoneal cancer is common, and there may be ascites from various causes. The ascitic fluid may be serous, hemorrhagic, or chylous.

Secondary gastric cancer sometimes results from a primary growth in the stomach, *e. g.*, a cancer of the cardia may follow upon a pyloric growth, or, again, a pyloric stenosis may occur from compression by periportal cancerous glands, which become involved from a primary cancer of the cardiac orifice.

The general morbid anatomy reveals, as in any other cancer, marasmus, with brown atrophy of the heart and fatty degeneration of its muscle, brown atrophy of the liver, fatty kidneys, and not uncommonly degenerations in the spinal cord and peripheral nerves. Multiple thrombi associated with the marasmus, or arising from the neoplasm are sometimes found. General anasarca, anemia, and cachexia are added.

Symptoms.—These vary according to the stage of the disease, the situation, the extent and pathological character of the growth, and upon its direction of progression.

Latency.—The onset may be quite unnoticed either by patient or physician and the disease may be an accidental discovery at autopsy. Patients with gastric cancer may enjoy apparent health for months, with undisturbed appetite and digestion, and with maintenance of strength and nutrition even when extensive metastases are present. Cases occurring elsewhere than at the orifices are especially apt to be latent, although in cancers of the cardia when no obstruction has yet occurred, and no tumor can be felt, the course may be unobserved. Sometimes these cases simulate pernicious anemia.

Onset.—Symptoms usually begin with inexplicable "dyspepsia," which does not respond to treatment. Following upon this are pain, loss of weight, and weakness, later vomiting, perhaps of blood, and the cachexia progresses to a fatal issue. The onset and persistence of dyspepsia in a man over forty years of age, who has previously enjoyed good health, is a suspicious circumstance. Sometimes the onset is apparently sudden, in the midst of health, or after some acute illness, or perhaps after a trauma. In one class of cases the onset is often characteristic, viz., where *cancer follows ulcer* or is engrafted upon it. In many of these the diagnosis is obscure through the presence of hyperacidity, especially as the HCl may be in excess to the end, and with it hypersecretion and early motor insufficiency; perhaps all the more so because spasm develops at the pylorus with the hyperchlorhydria. The deficiency of HCl in these cases appears late, and lactic acid is correspondingly small in amount and only found late. Pain and hemorrhages are early signs in these cases and usually marked features.

Early Digestive Symptoms.—*Flatulence* is frequent, at first odorless. Later on with degeneration or ulceration of the neoplasm, the expelled gas has a fetid or foul odor from gangrene, suppuration, or the presence of organic acids. A *sensation of fulness* occurs even after very little food. *Anorexia* is common and early, and is apt to be progressive, although in many cases unimpaired until late in the disease. The appetite often shows caprice and an especial dislike for meat may develop. The taste is altered and often perverted. Smokers commonly lose all desire for tobacco. Bulimia and dysphagia are rare. *Thirst* is definitely related to the degree of stenosis and to the motor insufficiency. The *tongue* is usually thickly coated, although at times clean for months; much depends on the condition of the teeth, gums and pharynx.

Vomiting.—This is very frequent, and occurs in 80 to 90 per cent. of all cases. It usually takes place late in the course of the malady, and is especially common in pyloric cancer, owing, of course, to the stagnation and dilatation. In Warren Lyman's statistics from the Royal Victoria Hospital, it was noted in 68.2 per cent. Sometimes it is early (in 7 out of 83 of our patients it was the first symptom, and in 34 it was very early). Acute fatal cases with rapid emaciation and repeated uncontrollable vomiting have been described. As dilatation becomes more pronounced the vomiting may be at longer intervals and then more copious, the vomitus being largely unaltered and mixed with mucus, blood pigment, detritus, etc., and having a foul or fetid odor from organic acids. Often three layers form in the vomitus when retention of food has existed, the uppermost frothy, the middle layer consisting of turbid fluid and partly digested foodstuff, while at the bottom there is a granular material with food in various stages of digestion and other matter foreign to normal digestion. When an ulcerating obstructive growth at the pylorus breaks down to create a new passage, the vomiting may cease for weeks and the motor insufficiency be temporarily relieved. Vomiting is much less frequent when the fundus or anterior wall is the original seat of the cancer. In 26 of our 83 cases, vomiting was either absent until death or until discharge from the hospital. When the cardia is

affected alone, vomiting will be more of the nature of a regurgitation and with much mucus. It is, as a rule, preceded by nausea, salivation and digestive discomfort. As a rule, vomiting causes some relief to the general discomfort, but not much to the pain.

Hematemesis.—This is common but occurs as an obvious sign in less than half of all gastric cancers. Chemical tests for occult blood, however, show hemorrhage to be much more frequent. It is important to distinguish between true coffee-ground vomitus and altered foodstuffs with a similar appearance. This can be determined often only by chemical tests, by the microscope or the spectroscope.

The bleeding may occur from erosion of a large vessel, and be copious and even fatal, although this is rare (1 per cent., Welch); death may occur from hemorrhage without emesis. More usually there are small repeated hemorrhages, either from the degenerated tumor, or from superficial erosion of the mucosa. The blood oozes slowly, remains a long time in the stomach, and for this reason it is altered to hematin, giving to the contents the coffee-ground appearance. Tiny specks of very dark clotted blood, which frequently appear in the vomitus with cancer of the lesser curvature, are of diagnostic importance, coming from folds of the mucous membrane or in depressions of the neoplasm. This is often a very early sign of cancer, especially if associated with the Boas–Oppler bacillus. The blood, though sometimes pure, is usually mixed with food. *Occult bleedings* are a very important finding, and form one of the most constant signs in the disease.

Pus is less commonly vomited, and if copious may be seen by the naked eye, or detected by its fetid odor. If in small amount, it may only be revealed by the microscope. It arises through degeneration and ulceration of the neoplasm, and its presence is important for diagnosis.

Pain.—This is usually preceded for a time by a mere sense of pressure and discomfort, especially after meals. It was the first symptom in 25 out of 83 cases in the Royal Victoria Hospital (31 per cent.), and was present in the gastric region in 75 per cent. In from 75 to 90 per cent. it occurs at some time during the progress of the disease. In Osler and McCrae's series 13 per cent. ran a painless course. In the Royal Victoria Hospital, 22 per cent. had no gastric pain (Lyman). The time of its appearance varies, sometimes only every few days or weeks, sometimes only at night, etc., while at other times it is constant. The degree of *intensity*, as a rule, is not excessive. There is painful distress or a dull ache, usually fairly well localized to the gastric area. Sometimes it radiates to the back and to the sacrum. If the cancer be at the cardiac end, the pain may be at the lower end of the sternum. In pyloric stenosis peristaltic, cramp-like pains occur, and there is a sense of unrest.

A relation between the presence of a tumor and the site of the pain does not necessarily exist. In some of our cases with diffuse infiltration of the stomach no pain existed, and pain was absent in at least one of each typical variety of regional disease. Cardiac cancer was especially free from pain. A relation to food may or may not exist.

The Bowels.—These are rarely regular and are usually constipated at first. F. Müller says that diarrhœa occurs in 35 per cent. of all gastric

cancers and at times the two conditions alternate. Occult blood is present in the stools in probably over 90 per cent. of cases.

The Urine.—The quantity is usually diminished and the urine is concentrated according to the degree of gastrectasis and pyloric stenosis. The *chlorides* vary within wide limits, and *phosphates* are increased. *Nitrogen* is increased because of the great albumin destruction that occurs in gastric cancer. *Albumin* is frequently present although usually in small amount. *Albumoses* (peptonuria) have been found from time to time and a certain diagnostic significance attaches to their presence. It is merely a confirmative test. *Indican and ethereal sulphates* are sometimes in excess and *acetone and diacetic acid* are sometimes present, and of no diagnostic import. *Volatile fatty acids* are in excess sometimes when cancer occurs with stasis and diminished HCl. The presence of *sugar* in the urine implies the probable involvement of the pancreas or brain and perhaps of the liver.

Nutrition.—Emaciation is the rule; it is usually progressive, and is often the first sign to arouse suspicion. The skin becomes lax and wrinkled, the color sallow, and sometimes jaundiced. Cachexia supervenes, especially with motor insufficiency. There is nothing pathognomonic about the cachexia. Two exceptions are worthy of mention: (1) Some patients run an advanced course with well-maintained nutrition. (2) Remissions occur, patients regaining some or much of their lost weight for a time, especially under careful lavage and diet, with encouragement. In cancer of the lesser curvature there is usually but little emaciation early in the disease. *Loss of strength* usually accompanies emaciation.

Anemia.—This is due to the toxemia, hemorrhage, and malnutrition, but the blood examination is of little value in the diagnosis. Usually there is moderate leukocytosis. The red cells are normal or much diminished, sometimes there is marked poikilocytosis, and the picture may resemble that of pernicious anemia. The hemoglobin is diminished. The average red count is usually about 2,000,000 per c.mm. The absence of digestive leukocytosis has no practical diagnostic value.

Fever.—This occurs in one-half or three-quarters of all cases, and at varying and irregular intervals. Sometimes there is an initial fever or irregular temperature during the course, and not uncommonly sudden elevations to 105° or 106° with rigors. As other times the type resembles that seen in malaria with chills and sweats. These irregularities are probably toxic, arising from absorption, if not due to complications, *e. g.*, peritonitis, pleurisy, etc. Terminal pneumonia or pulmonary metastases often cause fever during the latter days of the disease.

Adenitis.—The neck may show enlarged *supraclavicular* lymph glands, especially on the left side. They become swollen, palpable, perhaps visible above the clavicle. The diagnostic value of this is doubtful and it may occur in any visceral cancer. It is usually a late sign but sometimes it is early enough to be of use, and should be looked for.

The Abdominal Examination.—Inspection.—This is of great importance. Osler drew special attention to examination of the abdomen for unevenness of the furrows below the ribs, for fulness in the epigastrium, nodules in the skin and about the navel, peristalsis and anti-

peristalsis, and, lastly, for a wide area of aortic pulsation. It is well to inspect the recumbent patient from behind the head of the bed. The tumor is often easily seen as it descends with deep respiration, and ascends with expiration, especially when the stomach is empty. With a full stomach a tumor may be pushed upward beneath the ribs or liver and be invisible. *Respiration* often has a marked effect on the position of the tumor, especially if it be localized to the pylorus, circumscribed and solid, and with adhesions to the liver. It may be accepted as a genera lrule that absence of respiratory mobility implies non-adherence to the liver. Cancers of the curvatures move readily, and may show fixation on expiration. This aids in the differentiation both of cancer of the stomach from that of other organs, and of cancer of the pylorus from that of the lesser curvature. Often tumors which descend with inspiration may be held in that position during expiration. The changes of position depend on the size, the state, and the extent of the tumor. A large, wide tumor, adherent to the liver and yet extending below it, may be partly fixed even when the liver returns with expiration.

Insufflation and inflation have some influence on the situation of a neoplasm in the stomach. Inflation should be carried out with care. The writer saw a severe laceration of the mucosa result from it in a European clinic, where the autopsy revealed four or five linear tears from end to end of the organ. Pyloric tumors descend to the right, and those of the lesser curvature move backward and disappear because the larger curvature turns forward.

Palpation.—The examination should be made in various positi ons, and if necessary in a hot bath, or under ether, in order to determine the size, shape, and situation, mobility, character, etc., of the growth. In the absence of a palpable tumor, the diagnosis often remains dubious. Sometimes a tumor is not accessible to palpation even when large, especially if (1) it is high up in the cardia, (2) if it is in the lesser curvature and fixed to that vicinity, or under the left lobe of the liver, or (3) if it is in the posterior wall of the stomach. Tenderness is common, in variable sites, and there are often tender points behind near the vertebræ. It is often possible to feel a hardness and the nodular character of a neoplasm and the knobs of cancerous masses with central depressions of degeneration (Farre's tubercles).

Pyloric tumors are the easiest of all to palpate, especially in women with lax abdomens and descended stomachs. Not infrequently one may feel the gurgling of gas through the pylorus. These tumors are sometimes quite movable, especially if non-adherent and confined to the pylorus. Sometimes they may be moved to almost any position in the abdomen.

Gastric Rigidity.—Boas has drawn attention to this symptom, although Creveilhier noted it more than half a century ago. The rigidity may exist merely as slight contractions of short duration confined more or less to the fundus, or as more marked tonic spasms of the muscle over a larger area, causing prominences of the fundus, and creating a sensation of pain to the patient, or, again, there may be still more decided contractions, which are both visible and palpable and are of longer duration. Gastric rigidity implies pyloric obstruction, and it is best observed with a full stomach.

Percussion.—Dulness or dull tympany may exist over a large tumor. There is increased tympany with gastrectasis. Inflation aids mensuration.

Auscultation.—Auscultation and auscultatory percussion are of doubtful value. The sign of the deglutition sounds, viz., delay in their occurrence, is of doubtful value, and certainly not pathognomonic. It is possible to hear, too, the gurgling of gas through the pylorus. Friction from a localized peritonitis is sometimes audible.

The Functional Signs and Analysis of the Stomach Contents.—There is no one pathognomonic sign of cancer. The diagnosis is made from the symptom and sign complex. The signs vary greatly according to the site, size, and extent, shape, character, etc., of the neoplasm. Macroscopically the stomach contents show stagnation, fermentation, and poor protein digestion. Tumor fragments are rarely seen. Blood is common and sometimes there is pus. In typical cases three changes occur: (1) Motor power is impaired, (2) HCl is diminished or absent, (3) lactic acid is present.

The *motor power* is nearly always diminished early in all forms of gastric cancer and is a most important element in the diagnosis. It is not necessarily associated with dilatation, for a small rigid, cancerous stomach may equally well show motor insufficiency. It rapidly becomes more severe, especially with marked stenosis and insufficient hypertrophy of the muscularis. In cancer of the cardia it is less frequent than in cancer elsewhere. In cancer of the lesser curvature, motor insufficiency is slight at first until extension and infiltration have occurred, involving the pylorus, but not necessarily causing stenosis so much as preventing peristalsis and inducing a rigidity of the wall with insufficient pylorus. In cancer of the body of the stomach, more than 50 per cent. of cases show motor insufficiency because of the infiltration of the walls and their weakness through toxemia and cachexia. Where the wall is much infiltrated or where pyloric stenosis is marked, food may be retained for days or weeks and the increase is usually progressive. An authority recommends the examination of the fasting contents after the ingestion of powdered charcoal and milk twelve hours previously. In 30 out of 50 cases, residue was found, while other signs in the fasting contents were the presence of lactic acid—a high titre for fixed acids, foul odor, etc.

Secretory Power.—There is usually a gradual and progressive diminution of the free HCl until it is absent, and the ferments also disappear in part or entirely. This occurs in perhaps 80 to 90 per cent. of cases. One examination of the contents is never enough to form conclusions; it is the persistent diminution or absence of HCl which is significant. Variability in the amount of HCl secreted in gastric carcinoma is probably much greater than is commonly recognized, and the total acidity varies within still wider limits. Combined HCl is often absent. It is probable that much HCl is secreted but is quickly taken up by products resulting from the cancer. Emerson found that in ulcerating cancers certain basic substances were produced by autolytic processes, which combined with HCl. He believes these to be "hexone bases, the result of the digestion of the protein by a ferment furnished by the tumor itself." With cancerous dilatation we may get free HCl in an empty

stomach, but not after meals. Friedenwald and Bryan examined 100 cases of gastric cancer by fractional analysis. In 52 there was achlorhydria; in 16 hypochlorhydria; in 26 the findings were normal, and in only 6 was there hyperchlorhydria.

Hyperacidity with cancer of the stomach may occur early in the disease. The writer has observed repeatedly such cases in which the early hyperacidity lasted for more than a year before cancer was at all evident. In one of these cases the autopsy showed no sign of previous ulcer, but a carcinoma *en plaque*. In cancer of the fundus we get absence of HCl much earlier, because the process is more diffuse, and therefore affects the secreting glands more. In all cases one must distinguished between hyperchlorhydria and mere hyperacidity which is often due to organic acids as well. Hydrochloric acid may be present throughout the whole course, especially with localized tumors or when ulcer previously existed.

Absence of HCl is but one sign, and is of partial importance only; for it occurs, too, in gastric neuroses, catarrh, atrophy, etc., and in fevers, constitutional disturbances, cardiac disease, etc.

Organic Acids: Lactic, Butyric, Acetic.– The presence of *lactic acid* depends mainly on diminished motor power and lessened HCl, and therefore lessened digestion of albuminous foods, *i. e.*, lessened ferment activity because of atrophy of the glands. It may be introduced preformed into the stomach by the food, *e. g.*, bread, milk, fish, meat, etc., and for this reason Boas recommended a test meal of oatmeal and water. This meal is given after having previously washed out the stomach.

Lactic acid is formed in the stomach, however, only under abnormal conditions, and is the commonest organic acid found in cancer. Its origin may be from acid producing microörganisms, *e. g.*, the Boas-Oppler bacillus, or from some special ferment associated with the cancerous tumor. Lactic acid is not pathognomonic of cancer, and is present in other conditions, though rarely in so marked a quantity as in cancer. Its *early appearance* in cancer of the stomach, together with a *diminution of the total acidity*, even before any signs of stenosis, is very important. Its absence is no proof that cancer is not present. Usually it is not an early sign, because it depends in part on atrophy of the glands and motor insufficiency. Still, these do sometimes atrophy *early*, as the mucous membrane is sometimes destroyed even when a tumor is quite localized, and, *vice versa*, with extensive cancerous disease the mucous membrane may be preserved. Hence the variations in time of the appearance of the lactic acid. Its constancy is very suggestive, for the persistent presence of lactic acid is rare in other gastric diseases.

Ferments.—Hammerschlag, in 1884, examined 280 patients with gastric disease, and found the peptonizing power (according to his method) below 15 per cent. in only 32 cases, of which 26 were cancer. In these there was no albuminous digestion in 23, and in the other 3 it was below 15 per cent. Oppler found that HCl secretion and ferment activity ran parallel, indicating that diminution of the pepsin cannot be regarded as an early sign of cancer. It is, moreover, not always present in cancer, and, *vice versa*, is present sometimes in benign stenosis with gastrectasis and in neuroses. The presence or absence of secondary

atrophy of the glands is alone the decisive feature in the production of ferments. Early diminution of ferment production, even when HCl secretion is preserved, has been repeatedly observed.

Occult bleedings from the stomach or bowel should be carefully looked for as being one of the early and most important signs of gastric cancer. The benzidin test should be used. The importance of this sign in the diagnosis depends, however, on their persistent presence and on their association with gastric subacidity. If occult blood occurs in the stools, when HCl is present in the gastric contents, the diagnostic value is less, as ulcer produces similar results. If occult blood is not found in the feces, and there is gastric subacidity and good motor power, it argues against the presence of cancer.

Microscopic Examination of the Stomach Contents.—This is more or less valuable according to the period of the disease. Blood cells and pigment are commonly found. Pus cells vary in amount, and at least a few leukocytes can almost always be seen. The presence of blood or pus, or both, in the early morning lavage is of great significance. Bits of mucous membrane and of cancer tissue are not commonly found. A few cases are recorded, but being a late sign, this has but little value. The lavage water frequently has little shreds of torn mucous membrane, because the mucous membrane in cancer is friable. Examination of these shows widening of the submucous tissue at expense of the true gland layer, *i. e.*, glandular atrophy. It is often hard to be sure of this, however, because it depends upon which part of the mucosa accidentally comes away in the washings. A piece of tumor is the only single pathognomonic sign of cancer of the stomach. But this means ulceration, and therefore a late stage. Malkow found bits of tumor in the feces.

Boas-Oppler Bacilli.—These have been frequently found in the stomach contents in gastric cancer. They grow best on media to which blood is added. Hence they are frequent in coffee-ground contents. The average length of the bacillus is 6 to 8 μ, although it varies between 3 and 10 μ; sometimes it occurs in long spirals and continuous threads, 1 μ broad.

Schlesinger and Kaufmann demonstrated the formation of lactic acid from various forms of sugars by these bacilli, therefore they may be regarded as *one* of the excitors of lactic acid formation in the stomach, but only one; therefore they are not specific for lactic acid formation. They have been found in 22 out of 70 cases of gastric disease; of these 22, 19 were cancers and 3 presented other conditions. Their absence does not prove the non-existence of cancer. Heichelheim emphasizes the findings in gastric contents of clots of blood with these bacilli, in the absence of HCl, as almost pathognomonic of cancer. Ziegler called attention to the microscopic evidence of stasis as important in the early diagnosis of cancer, especially finding Boas-Oppler bacilli amid mucus which may plug the introduced tube, also food remains and numerous leukocytes.

Sarcinæ are uncommon unless free HCl is present; therefore, as a rule they are only present when the cancer has formed on an old ulcer. The presence of sarcinæ is no proof that cancer is not present, although if they are in abundance the diagnostic value is of some importance as suggesting a benign rather than a malignant condition.

Amœbæ and flagellata are found in cases of cancer of the stomach in which no stasis exists, but in which an alkaline reaction obtains on the gastric surface, *i. e.*, non-pyloric cases. Cohnheim thinks them an early sign, and that they are found before the ulcerating tumor has become gangrenous. Later they disappear.

Yeast cells sometimes occur. *Meat fibres* are found because of delayed and lessened protein digestion. *Starchy foods* may be abundant, but are found to be more digested than the meats. *Fats* are likewise present.

Diagnosis.—Inasmuch as extirpation early in the disease is essential to a cure, the earliest possible diagnosis is necessary for rational treatment, and one must endeavor to determine not only the location of the disease, but its extent, and the presence or absence of complications. When possible, a diagnosis should be established before a tumor is detected, although from surgical statistics even this is not essential for a radical cure. Many tumors, even though palpable, are sufficiently localized for removal, and even when fairly large, a successful resection has been accomplished. Many tumors feel larger than they really are, and *vice versa*. It does not follow that because a tumor is not yet palpable that the disease is in an early stage. Huge cancers with adhesions and metastases may have formed and be entirely covered and inaccessible to palpation, and, *vice versa*, an advanced condition may remain localized for a long time and grow slowly long after the diagnosis is made. Cheever, reviewing 336 cases, found that, in 30 per cent., early symptoms had not suggested gastric disease, *i. e.*, weakness, loss of weight, pallor, backache, constipation and anorexia; 62.6 per cent. were inoperable and 9.7 per cent. were suitable for radical cures. The operative mortality was 16.6 per cent.; 25 per cent. were well after six years.

The main evidence in the early cases lies in the findings of functional disorder. There is no single pathognomonic sign of cancer of the stomach, and one must consider the whole symptom-complex. In spite of all there are numerous cases in which it is quite impossible to make a diagnosis. One general rule holds in most cases, viz., *the absence of all gastric symptoms and signs is important evidence against cancer*. Penzoldt has well said that in individuals over forty years of age with gastric trouble, one should not rest until one has satisfactorily decided for or against cancer. Klemperer advocated that elderly patients in doubtful early states should be placed on a rest cure with a protective diet for several weeks. If improvement does not result, cancer may be strongly suspected.

General Signs.—When no tumor is evident one must rely on the age, the history, especially the onset in good health, the anorexia, especially for meats, the hematemesis, weakness and emaciation in spite of apparently sufficient food, the motor insufficiency, and the results of chemical analysis and other investigations of the vomitus and test meals, and upon the presence of persistent occult blood in the feces. In the stomach contents the cardinal features are evidences of motor insufficiency, the persistent diminution of HCl, the presence of lactic acid and of blood.

Tumor.—The possibility of palpating a growth depends much on the topographical conditions of the stomach and of the tumor, *e. g.*, cancers with adhesions, with extension upward of the growth, etc., may not be

accessible to palpation. Where tumor is evident, one is called upon to decide (1) whether or not it be gastric, and (2) if gastric, whether it be of a cancerous nature or otherwise.

Certain *general chemical and serological tests* have been recommended as aids in the early diagnosis of gastric cancer before a tumor is palpable, *although none of these has justified the claims originally made for them.* Apparently in gastric cancer there is a complete cleavage of proteins in the stomach, for the cancerous tissue contains ferments which decompose the peptones and polypeptids into amino-acids. The binding power due to this cleavage in a large part accounts for the absence of HCl. Salomon based his test on these general ideas, though the results cannot be regarded as of great value as yet.

Salomon's Test.—The stomach is carefully washed on the evening before testing, after a preliminary non-albuminous fluid diet for twenty-four hours. On the next morning the stomach is washed thoroughly with normal saline solution (400 cc.), the same fluid being repeatedly used and then tested by Esbach's and Kjeldahl's tests. More than 20 mg. of nitrogen to 100 cc. or 0.5 gm. albumin suggests the presence of cancer. In negative cases there should be little or no turbidity with Esbach's reagent, and the nitrogen by Kjeldahl's method is not greater than 15 mg. Some regard this test as useful in cancer of the lesser curvature without stenosis, unless the cancer has formed on an old ulcer, in which case the little HCl present would digest the albumin present. The test is probably of some value, especially as indicating an ulceration of the gastro-intestinal tract, although not necessarily differentiating malignant from benign conditions. It may assist in diagnosing cancer from chronic gastritis.

Raymond and Zizine, comparing the ratio of amino-nitrogen to the total nitrogen in the blood and urine, found a large increase of the amino-nitrogen in cancer over that of normals. Although similar findings occur in other cachectic states as with acidosis, internal suppuration and prolonged fevers, these can usually be readily differentiated. The increase comes from the breaking-down of the cancer. The Wolff-Junghaus test is regarded by Brown as more helpful than Salomon's in differentiating between malignant and benign achylia but is only of moderate value.

O. Reissner's contention that the diagnosis is aided by the determination of the chlorides in the stomach contents, is worthy of mention. In gastric carcinoma the chlorides are apparently much increased, despite the fact that HCl is itself deficient, the alkaline cancer juices evidently themselves containing the chloride excess. The method of Lutke-Martius is employed, and while in other gastric diseases 100 cc. of gastric contents have a corresponding chloride value of 24 to 40 cc. of $\frac{N}{10}$ silver solution, in carcinoma 50 to 70 cc. of $\frac{N}{10}$ silver solution are required.

The Blood-sugar Content.—Friedenwald and Grove found high values during fasting, and, after 100 gm. of glucose, still higher figures, which remained on a high level for an abnormally long time. We believe this test to be of early diagnostic value.

Serum Test.—Abderhalden's early pregnancy test, as modified and carried out by Bruére and Hardisty at the Royal Victoria Hospital, may be considered useful for certain cases of carcinoma. The cancer

must be of such a size as to have caused a generalized blood reaction, *i. e.*, with antibodies or ferments in the blood. Pregnancy should be excluded. About 15 cc. of the patient's blood is drawn while fasting. No syringe should be used, but the needle placed in the vein should permit of the blood flowing into a sterilized tube under careful aseptic precautions. The blood is placed in the thermostat for five or six hours until the serum is well separated and the hemoglobin is removed by careful centrifugalization. Three hydrometer tubes are taken and sterilized. Into one 20 cc. of chloroform water (1 to 200) is added. A suitable parchment thimble (4 dialyses) is inserted, so that its surface comes in contact with the fluid. Into this thimble is placed 1 grm. of antigen, and 2 cc. of serum. If cancer be present a decided reaction should occur at the end of twenty-four hours. The other two hydrometer tubes are used as controls, placing into one of them 2 cc. of saline, instead of serum, and into the other 2 cc. saline with 2 cc. of serum (*i. e.*, without the antigen). All three tubes are carefully plugged and placed in the thermostat for twenty-four hours. The diffusates are each tested with ninhydrin for protein bodies. A positive reaction is indicated by the presence of a violet-blue color, which must be very decisive in order to call the reaction positive.

The Roentgen-rays.—The roentgen-rays are the most valuable aid in the diagnosis of cancer of the stomach. Ninety-five per cent. of all gastric cancers coming to operation in the Mayo Clinic had been previously diagnosed by the roentgen-rays. This figure, however, must vary according to the stage of the disease, the skill of the examiner, and other factors. It is obvious that in a very large percentage of cases, the early stages of cancer are not recognizable, the roentgen-ray signs depending upon the presence of sufficient infiltrative ulceration, obstruction or deformity.

Filling defects are the most important findings in radiological examination. These are encroachments on the gastric lumen and are characterized by their irregularity of outline and by the lack of symmetry between the edges of the gastric shadow. The patient must be placed in various positions to ensure a view of all the gastric contours. Filling defects should be single or multiple. If situated on the anterior or posterior wall, they may cause a transparency or translucency in the gastric shadow. If placed high in the cardia, the opaque meal must be manipulated, and the patient so postured that the cardia may be filled so as to demonstrate the presence of a filling defect. To be of diagnostic value, a filling defect must be permanent and survive all manipulations.

Pseudo-filling defects may be caused by extra-gastric pressure from other organs, from tumor, from a convex spine, etc. *Intragastric filling defects* are associated with the presence of foreign bodies, such as hair-balls or food material, or result from spasm. The inconstancy and movability of these defects under manipulation and posturing indicate their nature and origin.

Cancer of the pylorus may be obstructive in effect or may cause a wide open, gaping pylorus. Again, obstruction may be compensated by incompetence of the pylorus. A patulous pylorus is usually associated with infiltration of the cancer which interferes with the action of the sphincter.

In such cases the stomach empties almost immediately, and the characteristic picture is presented of small bowel patterns. Mills has shown that with an obstructive cancer of the middle portion of the stomach, there occurs an evulsion of the cardiac and pyloric sphincters, with a resulting incompetence and regurgitation of the barium both into the œsophagus and duodenum. Gastric syphilis frequently shows a similar picture.

Peristaltic changes are always found in cancer of the stomach and are a very important feature of the radiological diagnosis. When obstruction of the pylorus occurs, there will be peristaltic and antiperistaltic waves, varying in depth according to the degree of obstruction. The antiperistaltic movements begin in the pars pylorica and run upward in diminishing intensity until they are lost in the fundus. All degrees of motility, from complete obstruction to very rapid emptying, are found in gastric cancer. A complete or partial obstruction must be differentiated from that due to swelling and cicatricial contraction around the pyloric ulcer. While this is often impossible by the roentgen-rays alone, the clinical elements usually decide the doubt. In some instances this is not difficult, as for example, when hypermotility accompanies a duodenal ulcer, or when the achylia, with a patent pylorus, will be differentiated by other clinical findings. Lessened mobility of the stomach, while not a pathognomonic sign of cancer, is of great importance, indicating an extension of the growth outside of the stomach and its inoperability.

Alteration in the size or the shape of the stomach must always arouse suspicion of cancer. Infiltrating cancers of the scirrhous type induce a shrinkage of the organ, with diminution of size and alteration in the shape. The scirrhous type usually presents the gaping pylorus and a quick emptying stomach, while the medullary type, presents large filling defects and obstructive symptoms.

Differential Diagnosis.—Two main conditions may be considered: (*A*) Gastric cancer without tumor. (*B*) Gastric cancer with tumor.

A. Where no tumor can be detected, two classes of cases exist: (1) Those with little or no motor insufficiency. (2) Those with definite gastrectasis. (Cancer at the cardiac orifice is dealt with separately.)

1. Where no motor insufficiency exists, the cases are easier to diagnose if lactic acid is found, for it is rare in the other gastric diseases that have no atony. The main diseases in this group are:

(*a*) *Ulcer* without tumor or stenosis.

(*b*) *Neuroses.*

(*c*) *Chronic Gastritis.*—The history of a cause (alcohol), the gradual onset and slower progress, with remission and exacerbations, are important features. The secretions are disturbed later in the disease, and the features are more local than constitutional. Hydrochloric acid is less constantly absent and is often diminished. Motor insufficiency is later, progresses less rapidly, and there is less gastrectasis; there is also less stagnation and occult bleedings are less persistent, if at all present. There is no filling defect.

(*d*) *Atrophy of the mucous membrane* (including pernicious anemia, primary atrophy of the gastric follicles, terminal stage of advanced chronic gastritis, cancer of distant organs, Addison's disease, etc.).

2. *Cases with gastrectasis* are harder to differentiate, because the lactic acid is so often present in gastric diseases with atony (other than cancer), and therefore its presence has less significance. The roentgen-ray findings are of prime importance in the differentiation.

The main diseases to be differentiated are: *Scarred ulcer of the pylorus without palpable tumor* (which may lie beneath the liver or be too small for palpation). The history of previous ulcer, the longer duration of the malady, the presence of HCl (perhaps even in excess), the absence of lactic acid, the eructations of gas containing H_2S, and the findings of sarcinæ, all suggest the benign condition; and the absence of cachexia aids in excluding carcinoma. Hypertrophic stenosis of the pylorus (Boas' stenosing gastritis) if acquired, is usually due to ulcer and gives signs similar to the above. Sometimes *a carcinoma developing on an old ulcer* must be differentiated, and the diagnosis is not always easy; indeed, often it is quite impossible. As a rule, there is a history of old ulcer and the symptoms change in character, becoming more persistent and resistant to treatment. There is, however, greater wasting, anemia and pain. Bleeding and perforations are not uncommon. HCl is present, often in excess, and there may be hypersecretion (continuous or alimentary). Gluzinski's tests are perhaps useful in these cases; at all events, if positive, they indicate the presence of cancer, and if negative, they do not prove its absence. Cancer developing on an ulcer shows a tumor more easily because of the usual perigastritis and pyloric spasm.

B. When Tumor Exists.—Two questions arise: (1) Is the growth gastric or extragastric? (2) If gastric, is it benign or malignant? The roentgen-rays usually afford a satisfactory answer to the first. One must use careful palpation, if necessary with the patient in a warm bath or under ether, unless, indeed, an exploratory laparotomy be undertaken. Inflation or distention of the colon with water displaces gastric tumors upward, as also those of the spleen. Tumors of the kidney disappear behind an inflated colon. Tumors of the liver vary according to size and position, while those of the omentum are displaced downward.

Growths Located Outside the Stomach.—The tumors simulating gastric growths, but existing in reality outside the stomach, are mainly:

1. *Perigastritis*, with an exudate and perhaps adhesions about the pylorus, or the lesser curvature, may induce chronic pain with dyspepsia and even dilatation, simulating cancer. The main features against cancer are the long duration without sufficient corresponding emaciation and cachexia, the different chemical signs on analysis and the skiagraphic differences. (See "Complications of Gastric Ulcer.")

2. *Cancer of the Duodenum.*—This condition is rather rare. Schlesinger found only 7 primary cases in 25,000 histories. Rolleston could collect only 41 cases in the literature; of these, 8 were in the first portion, 5 in the first and second parts, 24 in the second portion, and 4 in the third portion of the duodenum; 10 were in females and 31 in males. Here the difficulties are great indeed; it may be impossible to diagnose the true condition. One may have diminution or absence of HCl. Lactic acid, on the other hand, may be present, as, indeed, may most of the other signs of gastric cancer.

3. *Omental or general peritoneal tumors* often cause difficulty, especially if accompanied by ascites. These neoplasms are less mobile with respiration, and the gastric analysis usually gives negative results. The rectum should always be examined in doubtful cases of the kind.

4. *Peritoneal tuberculosis* with ascites may simulate gastric cancer with secondary peritoneal involvement. However, it occurs usually in younger subjects, runs a more protracted course, with exacerbations and remissions, and is accompanied by more persistent irregular fever. No occult bleedings occur. Dock has drawn attention to the value of cytological diagnosis of the fluid with its characteristic cells, in which mitoses are very common.

5. *Tumors of the transverse colon* usually give evidence of some degree of intestinal obstruction; the stools may be bloody and examination of the stomach itself is negative.

6. *Tumors of the gall-bladder* are situated in their appropriate place, are somewhat movable, and may by pressure upon the ducts cause early jaundice. At times, however, the differential diagnosis is extremely difficult. Adhesions may cause pyloric stenosis and certain signs of gastric cancer. The absence of respiratory mobility may suggest a gastric cancer rather than one of the gall-bladder; but a test meal is negative.

7. *Cancer of the liver* is usually secondary, and the tumor is less easily fixed with expiration than are tumors of the stomach. A satisfactory means of differentiating is, where possible, to place the hand above the tumor. Then, if the liver can be felt still higher, the tumor is probably gastric; at all events, it is not hepatic. The same is true if, with inflation of the stomach, the tumor alters its position. When the cancer of the liver is primary, the liver becomes large rapidly; jaundice is early and pronounced. The gastric signs are slight or absent, and there is no hematemesis or gastrectasis, Moreover, the usual signs after a test meal are not found.

8. *The pancreas*, either normal or pathological. When normal, it is deeply situated in the median line, fixed and immovable with respiration, and disappearing upon inflation of the stomach. When it is diseased, and especially when it is the seat of a cancerous growth, one may find clayey, fatty stools, even without jaundice. Jaundice may be present from pressure of the growth upon the common duct. The portal vein may be pressed upon, resulting in ascites. There may be glycosuria, and, as a rule, the course is a rapid one. Armstrong reported a case in which a large pancreatic cyst simulated cancer of the stomach, even to the gastric analysis. The stools had not been observed.

9. Other conditions which may simulate a gastric tumor are gumma of the left lobe of the liver, aneurism of the abdominal aorta, swollen glands about this artery, a movable kidney, and enlarged spleen, the last simulating a cancer of the fundus.

Tumors within the Stomach.—*Gastric tumors* arise either from carcinoma or sarcoma, cicatrized ulcer of the stomach or duodenum, with or without a perigastritis, thickened or spastic pylorus, fibroma, lipoma, or foreign bodies (hair ball, etc.). The differential diagnosis depends upon the history, the symptom-complex, and the physical examination:

1. *In scarred pyloric ulcers*, stenosis and gastrectasis occur with the results common to all cases of pyloric obstruction, but the history of previous ulcer, the long duration, the presence of a smoother and more movable tumor, the character of the vomitus with proteins well digested, and chemical findings typical of benign stenosis, usually render the diagnosis clear. There are, moreover, no metastases.

2. *A hypertrophic stenosis of the pylorus* is usually acquired, but occurs, however, oftenest in early infancy. The cases late in life usually have diagnostic features common to scarred pyloric ulcers with obstruction, with which, too, they have usually a causal connection. Simple hypertrophy is undoubtedly rare. Sometimes it occurs with mere hypersecretion. One relies on the history and duration, the chemical analyses, and absence of general signs of cancer. Occasionally it may be impossible to differentiate the two conditions.

3. *Spasm* of the pylorus may possibly induce gastrectasis, and if so will manifest few if any of the signs of malignant disease. The condition will be of long duration, with exacerbations and remissions, and will present no chemical signs in the gastric contents of malignant disease nor occult bleedings in the stools.

4. *Fibromata and lipomata* can only be inferred and not definitely diagnosed in the present state of our knowledge.

Regional Diagnosis of Tumors within the Stomach.—Certain differential features are useful to determine *the exact site* of the neoplasm.

Cancer of the lesser curvature usually presents achylia from the beginning. There is less motor insufficiency until cancerous infiltration occurs, and then the fluorescent screen will show the fixation. Peristalsis is absent, but one may get tonic contraction of muscle (gastric rigidity). When the neoplasm extends to the pylorus, we get a rigid patulous pylorus *i. e.*, a paradoxical condition of atony with pyloric insufficiency, which may be tested by inflation. It is usually a late sign. Cancer of the lesser curvature is palpable only if ptosis exists or if the tumor has attained a considerable size. The weight is often maintained for a long time, because there is no obstruction.

Cancer of the Cardiac End.—Statistics of the Middlesex Hospital (1854 to 1904) recorded 227 cases of cancer of the stomach, of which 19 had their origin at the cardia; 13 were in males and 6 in females. Certainly it is uncommon, and many cases supposedly originating in the cardia probably commenced in the œsophagus. The type of cancer originating at the cardia is usually adenocarcinoma. Sometimes a cardiac cancer with stenosis is accompanied by separate cancer of the pylorus, and sometimes, too, cancer of the cardia is accompanied by a secondary stenosis of the pylorus from pressure of metastatic periportal glands.

Symptoms of Cancer at the Cardia.—Being usually inaccessible to palpation they remain latent for a long time. An interesting example under personal observation occurred in a man, aged forty-eight years, whose death occurred within four weeks of the onset of the symptoms. His earliest symptoms were abdominal distention, swelling of the left leg, and some weakness. For three weeks he had felt general abdominal pain with some anorexia, but there had been no other subjective evidence

of gastric disease. At the end of three weeks there was enormous distention from ascites, and he died two days later. The autopsy revealed a primary cancer of the cardia, with secondary involvement of the peritoneum.

Apart from the general signs of malignant disease, there is dysphagia and distress immediately after meals with regurgitation of food and mucus. Pain comes on at once after food, and is usually greater in this form than in cancer of the pylorus, and often there is tenderness on percussion or pressure over the xiphoid cartilage. As obstruction develops at the lower end of the œsophagus, there is at first some difficulty in the ingestion of solids, and their deglutition is assisted by liquids. Oppression and discomfort usually supervene. Later on, even soft foods are swallowed with difficulty, and finally only liquids can be taken into the stomach. When the obstruction is greatest, all food is ejected with retching. Vomiting is less frequent than mere regurgitation. The passage of a tube meets with an obstruction near the cardiac orifice. The withdrawal of blood on the end of the tube is of great diagnostic value. Motor insufficiency is usually slight and lactic acid fermentation need not exist. The delay of the deglutition sounds is not a reliable sign.

Course and Duration.—Dyspepsia, loss of flesh, pain, and vomiting, in the order mentioned, mark the progressive course of the malady. As a rule, the disease has few or no remissions, and the progress to a fatal ending is uninterrupted. Sometimes temporary improvement, both subjective and objective, occurs with marked gain in weight, color, appetite, and even strength. These ephemeral remissions often render the differential diagnosis from chronic gastritis most difficult. Sometimes there is an acute rapid course with vomiting, and a fatal termination in a few weeks, with carcinosis.

The *duration* varies according to the nature of the neoplasm, its site and extent. Non-obstructive scirrhus cancers are the slowest to develop, while medullary cancers and those causing stenosis of the orifices proceed more rapidly. Some authorities regard the cases which occur in youth as being especially rapid, but statistics do not all bear out this view. The average duration in cancer of the stomach is about one year, although some patients live longer than three or even five years. Death occurs from marasmus, metastases, or complications (hemorrhage, perforation, peritonitis, sepsis, pneumonia, etc.).

Prognosis.—This is always extremely grave. The medical treatment is purely symptomatic, and permanent relief is only to be had from complete resection of the growth. This is unfortunately possible in but a limited number, although with earlier diagnosis and better surgical technique, the hope of cures shows a satisfactory advance in the last five years out of all proportion to the gains in all previous years.

Treatment.—Medical.—This varies chiefly according to the situation of the growth and the functional signs. While the radical treatment is essentially surgical, there is much to be said for the medical treatment, which may be of great benefit, even though it cannot in any sense cure. The cases may be divided into (1) those with obstruction at the cardia, (2) those with pyloric stenosis, and (3) those in which no orifice is involved, but the body of the stomach is the main site of the neoplasm.

In *cancer of the cardia*, especially with the development of obstruction, soft or liquid diet is essential, and solids should be avoided. Small amounts with frequent feedings are better than large meals, and will better prevent regurgitation, pain, and distension of the œsophagus. Mechanical treatment plays but little part, and the use of a sound for therapeutic purposes is of questionable value. There is great danger of increasing the distress by injuring the parts, although if a tube of proper size and consistence be carefully employed it sometimes gives freer passage to food for a time and relieves symptoms.

In pyloric stenosis with gastrectasis the diet should not be too restricted. As a rule, liquid foods which are easily assimilated are best borne. But one should be largely guided by general principles, consulting the preferences of the individual. The meals should be small, frequent, and non-irritating. Hydrochloric acid being usually deficient, meats and albuminous foods should be restricted. When administered they should be finely divided, and free from cartilage and other ingredients difficult of digestion. White meats are preferable, chicken, game, and pigeon, also veal and beef in small amounts, and fish. It is well after the use of proteins to give small quantities of dilute HCl (unless HCl be present in the gastric secretion). Fleiner recommended the use of sauces containing HCl, *e. g.*, beef juice with warm water, to which dilute HCl is added. This cannot duly replace the deficiency, yet it often aids digestion. The same may be said of pepsin and pancreatin, which may give a sense of comfort to the patient. Instead of HCl, some use phosphoric acid after meals. If pain is present, small doses of codeine may be added.

It is a delusion to believe that the liberal use of albuminous foods prevents decomposition of the albumin of the body. The more a cancerous patient gets, the more he destroys.

The finer vegetables, preferably mashed, may be used in relatively large amounts, avoiding those with shells, skins, fibres, etc., as also those which induce much fermentation. Stale bread may be allowed, as also gruels, vegetable soups, and thin, farinaceous preparations like rice, macaroni, barley, tapioca, sago, and oatmeal. Stewed fruits are also well taken. Milk with coffee, cocoa, cereals, etc., may be employed, as also buttermilk and koumyss. Infant foods are often taken with relish and should be tried. Butter is the best borne of all the fats.

As beverages any of the ordinary drinks may be given, but in limited amount because of the motor insufficiency, and also light wines, brandy, and whisky in small amounts and diluted. Thirst is often troublesome and if not relieved by the moderate use of fluids, saline enemata may be used, one-half to one pint being injected night and morning.

The Mechanical Treatment.—Lavage with plain water, as a rule, alleviates the distressing local symptoms, and may help to increase the appetite and stimulate the secretions. The washing should be thorough at each occasion and unless gastrectasis be extreme, one lavage daily will suffice, before the last small evening meal or in the early morning. Some introduce 2 or 3 ounces of warm oil through the tube after the completion of the lavage, giving relief to the local distress.

In cancer of the body of the stomach, where motor insufficiency is but little evident, the main treatment is dietetic, the food being administered as in pyloric stenosis. Mechanical treatment is less indicated.

Medicinal Treatment.—No medicine is of any great value. Alkaline mineral waters before meals sometimes stimulate the secretions, while HCl after meals helps protein digestion. For the *vomiting,* especially of blood, rest to the stomach is essential. Nutrient enemata may be given, and then careful feeding by mouth may be begun with small quantities of fluid. For the ordinary vomiting, lavage is the best form of treatment.

Diarrhœa should be treated by a proper diet when possible, and by the use of lavage to remove irritating substances, which are the probable cause of the condition. For the *constipation,* aloes, rhubarb, and cascara are the most effective remedies. Enemata should be given when the condition is aggravated, but these should not be continued for too long a time. Authorities differ as to the use of saline purgatives, and doubtless in individual cases their use will have different effects.

For the *pain* wet compresses upon the stomach, lavage, and the use of spirit of chloroform may be of value, and it is only in the extreme cases that morphine should be employed.

Roentgen-ray Treatment.—Apart from the relief of pain and occasional temporary arrest of other symptoms, the newer methods of treatment by roentgen-rays have not been productive of satisfactory results. For inoperable cases suffering great pain, we are in the habit of using a fractional dosage of deep therapy, with high voltage, at the Royal Victoria Hospital, and in many instances, the suffering is temporarily relieved. *Radium* has been equally unsatisfactory, though occasionally, after removal of a cancerous tumor, the insertion of radium seeds prevents a more rapid recurrence. It is doubtful if cases are healed thereby.

Surgical Treatment.—Statistics of surgical treatment are still to be regarded with reserve. Alexis Thompson emphasized the frequency of non-malignant fibromatosis simulating cancer, thus exposing many of the difficulties of diagnosis and inaccuracy of reports on surgical "cure" of cancer. Two measures must be considered: 1. *Exploratory operation for diagnosis,* and not merely to confirm the diagnosis. When a tumor is present and the gastric analysis gives every indication of cancer, it is but idle curiosity to explore, unless some chance of giving relief exists. The object of exploration is to *make* the diagnosis when great suspicion and doubt exist as to the possibility of cancer. If in such cases a reasonable suspicion exists, the earlier discovery by an operation gives the patient a better chance of radical surgical cure, and as such, exploration is not only justifiable but advisable. Delay under these conditions, to await further evidence, is unnecessary waste of time. At other times it may seem uncertain (even when a tumor is palpable) whether extirpation is possible, and under these circumstances exploration is justifiable.

2. *Operation for treatment,* either curative or palliative. The cases which promise successful results are as follows: (1) Those in which the neoplasm is well localized and movable. One should be guided chiefly by the character and extent of adhesions, those which are not extensive and uninfiltrated being most satisfactory to deal with. Hence,

Ewald's contention that one must explore before deciding on further operative interference. (2) In the stomach itself the course of the lymphatics has an important bearing on the prognosis and treatment. The studies of Cunea have shown that the lymphatics along the lesser curvature run for the most part from the pylorus *toward* the cardia, while those along the greater curvature and fundus lead toward the pylorus. Thus in operations for gastric cancer, the extent of removal depends largely on the site of the growth. Pyloric cancers do not tend to spread to the fundus and greater curvature, and these parts, therefore, do not need to be included in the resection. On the other hand, the lesser curvature should be removed, at all events as far as the gastric artery (Mikulicz's point), and along the greater curvature as far as Hartmann's point, which delimits the lymphatic extension along that line (Hartmann-Mikulicz line of section). Toward the duodenal end, the resection should be made one inch clear of the pylorus, this being the extreme limit of secondary involvement in nearly all cases. Even in cancers of long duration the neighboring glands are sometimes left free. Resection relieved symptoms for three years in 37 per cent., for five years in 25 per cent. and for ten years in a few cases. Operative mortality was, on the average, 14 per cent.

Special Considerations.—Infiltrating adhesions are a contra-indication and a dangerous complication in operations. It has been estimated that 73 per cent. of such cases die, and the remaining 27 per cent. recover because the adhesions were slight, and probably non-infiltrating.

The Size of the Tumor.—The fact that a tumor is externally palpable is no longer regarded as a contra-indication to surgical treatment. In fact, the size of the tumor is less important than is the presence of adhesions. Many large tumors may be capable of successful removal because they are free from adhesions and metastases, while many small primary tumors may have involved neighboring glands and organs. Metastases in the liver may be large and numerous even when the primary local gastric neoplasm is small, movable, and non-adherent.

Complications form another important contra-indication, *e. g.*, arteriosclerosis, fatty heart, and tuberculosis.

Statistics showing the duration of life after operations of various kinds have no value as regards the selection of operation. Immediate results depend largely on the technique and the condition of the patient at the time of operation, both of which factors determine the success of operation and the ultimate duration of life. The only operations which are curative are those which remove the entire diseased parts.

Methods.—Gastrectomy was first successfully performed by Billroth in 1881, when a partial operation was done, while complete removal of the stomach was first attempted by Connor, of Cincinnati, in 1883, who, although unsuccessful, paved the way for the results of Schlatter, of Zurich, in 1897, who performed a complete gastrectomy with recovery. The œsophagus and jejunum were united and the duodenal opening closed. Since these early operations, a considerable advance has been made and in suitable cases satisfactory results are sometimes recorded. Successful

partial gastrectomies result in improved motility, and occasionally the HCl secretion returns. Choyce is of the opinion that partial gastrectomy should be carried out whenever possible, and that it is even justifiable to exercise a portion of the liver where the pylorus is adherent to it. In skilled hands the operative mortality is not high. Choyce's records give 6 deaths in 84 cases. The remote results are equally encouraging, 21 of 84 cases were free from recurrence after three years, 3 after more than 10, and 4 after more than six years. The average duration of life after partial gastrectomy in cases with recurrence was about eighteen months and the quality of life was good. In one of the late Dr. Garrow's cases, with very marked disease, the patient is living after fifteen years.

Remote Results.—Evidently the mechanical, physiological, and chemical functions of the stomach can be taken up by the parts left behind. Sometimes the œsophagus or small bowel dilates to form a kind of reservoir. Digestion is carried on well by the intestinal juices and pancreatic and hepatic secretions, and absorption takes place in an apparently satisfactory manner, and thus perfect health is maintained.

Palliative surgical treatment is employed in some inoperable cases when the strength of the patient permits. Cure is not aimed at, but merely a relief of certain symptoms and fulfilment of certain requirements for improvement of local and general conditions. The indications for gastro-enterostomy are, briefly, pyloric stenosis from a cancer which cannot be removed, hour-glass or other deformity involving stagnation of food and its complications, hemorrhage which is persistent, and uncontrollable vomiting, whether from retention or from general causes. It is further indicated in some cases as a temporary measure prior to the more serious operation of gastrectomy, when patients are too weak to undergo the latter operation immediately.

In any doubtful cases with adhesions to the neighboring organs or pressure of inflammatory tissues about the pylorus, a gastro-enterostomy may not only relieve, but cure. In a case reported by my colleague Garrow, a large indurated and nodular mass was found at operation involving the pylorus. It had been tucked up underneath the liver, and was not palpable; a second mass extended along the lesser curvature, while the glands in the lesser omentum were enlarged, although not indurated, as was the mass in the pyloric region. The condition was regarded as undoubtedly cancerous and a palliative gastro-enterostomy was performed. One year later the patient was in excellent health, suggesting the probability of some lesion other than a malignant one. Operation should be delayed when there is little gastric disturbance and when there is great weakness. Cases with small stomachs and infiltrating cancers should be let alone.

The beneficial results of gastro-enterostomy are often marked. Patients may gain in weight, the appetite may increase, vomiting and pain diminish, and general improvement follow for some months. Comparative comfort may thus be attained. In other cases, however, results are discouraging and the patients decline rapidly; the rapidity of growth in the neoplasm is marked, even closing the artificial opening.

Gastrostomy is indicated when food cannot be properly taken into the stomach from cancer of the œsophagus or of the cardiac end of the stomach. The operation should be done early to obviate the great weakness resulting from defective nutrition.

ACUTE GASTRITIS

Definition.—An acute inflammation of the gastric mucosa with varying degrees of local and constitutional disturbance.

Classification.—Various types exist dependent upon the different etiological factors. Clinically there are three main types: (1) Acute simple gastritis (primary and secondary). (2) Phlegmonous gastritis. (3) Toxic gastritis (mild and severe). *Anatomically* one may add two other forms: (4) Mycotic gastritis. (5) Diphtheritic gastritis.

Acute Simple Gastritis.—Definition.—This is an acute catarrhal inflammation of the gastric mucosa, frequently accompanied by excessive secretion of mucus, desquamation of epithelium, and a resulting disturbance of digestion.

The condition is more often wrongly than correctly diagnosed, and in numerous instances a functional disturbance with slight temporary atony, or a neurosis, is misnamed gastritis. The term *gastritis* should be restricted to those patients in whom definite evidence of gastric inflammation exists, and should not be applied to temporary disturbance of function resulting from slight indiscretions in diet. Certainly one often cannot decide clinically whether or not a true inflammation exists, for there are very few pathognomonic symptoms and signs of a mild simple gastritis. The autopsy room reveals often enough an acute inflammation of the gastric mucosa without a previous history of gastric symptoms, and, *vice versa*, where much disturbance of digestion may have occurred and when even much mucus has been secreted, the inflammatory lesion may be very slight indeed.

Etiology.—The condition is either primary or secondary.

Primary Acute Simple Gastritis.—Predisposing and direct causes exist. The former are numerous: faulty hygiene, the hot summer season, malnutrition, anemia and other circulatory disorders, constitutional and metabolic disturbances, and infectious diseases. Previous chronic gastritis predisposes to acute attacks. Individual susceptibility is an important factor, and perhaps heredity plays a part. Age, too, has much to do with susceptibility, infants being peculiarly liable.

The direct causes are mechanical and dietetic, thermal, chemical (toxic), or parasitic (vegetable or animal).

1. *Mechanical causes* are mainly associated with errors in diet, *e. g.*, irritating food or drink, too bulky or coarse food, or excess after prolonged fasting. Food when taken in too large an amount may remain undigested, and induce fermentation or putrefaction, so, too, the shells of some vegetables, the stones and rinds of fruit, foreign bodies, hair, etc.

2. *Thermal Causes.*—Food and drink if at extremes of temperature may induce gastric catarrh, so also the external application of heat and

cold; and extensive burns on the body. Whether or not "cold" is a cause in itself is doubtful.

3. *Chemical causes* are perhaps the most frequent. Alcohol is the commonest factor and leads to the disease in its most typical form. Those unaccustomed to alcohol are the most liable, and the inflammation arises either from irritation from the amount taken, or in the case of some wines because of the acid produced by acetic fermentation. In children unripe fruit is a common cause. Any chemically strange substance if toxic, in strong enough concentration and of sufficiently irritating character, will induce a gastritis, *e. g.*, alcohol, acids, alkalis, salts of the heavy metals, calcium chloride, and certain drugs, *e. g.*, salicylates, the bromides, iodides, arsenic, mercury, phosphorus, copaiba, etc.

Decomposed *pus*, as in gangrene of the lung when the irritating sputum is swallowed, and, indeed, any decomposed albumin may directly or indirectly induce the disease. *Foods* if tainted or decomposed ("crapulous gastritis") bring about an inflammation directly through the action of fermentative or putrefactive agents; so also does stale beer. *Toxalbumins* form another group of agents. Such agents may be denominated as autotoxic causes, and are present in numerous diseases, (uremia, diabetes, gout, cholemia, and also in burns).

4. *Parasitic Causes.—Vegetable Parasites* (*Bacteria*).—The invasion of bacteria is one of the most common causes of acute gastritis—hence its frequent presence in the various acute infections. The colon bacillus is one of the most frequently found organisms, and when it occurs in the course of acute infections is often regarded as the cause of the secondary gastritis. In all such instances the origin of the gastritis may be largely chemical, and due to the products of the bacteria. An epidemic form of gastritis has received attention. This ill-understood condition is regarded as originating in some form of microbic infection. This "gastritis infectiosa" is regarded by some as a special disease.

Animal parasites are commonly associated with a true gastritis, although it is by no means a necessary feature of parasitic invasion of the stomach. The ascarides, the tænia, and even the oxyurides may induce an accompanying simple catarrh of the gastric mucosa, as may also the diptera, flies, and larvæ of various kinds.

Secondary acute gastritis develops in the course of many infectious diseases, and may be the main initial symptom, especially in children. In pulmonary diseases when degenerated or decomposed tissues and exudates are introduced incidentally into the stomach an acute catarrh results. Ellis records a hemorrhagic gastritis due to a swallowed laryngeal pseudomembrane, which also obstructed the pylorus. As an accompaniment of various intestinal diseases, acute renal and cardiac disease, etc., acute gastritis is not uncommon.

Pathology.—The size and shape of the stomach are not usually altered. There is a more or less diffuse redness and swelling of the mucosa, with congestion or patchy hemorrhages and an excessive quantity of mucus. The pyloric region is most frequently involved.

Microscopically, muciparous, cylindrical epithelium covers the free surface of the mucous membrane as well as the relatively deep stomach

cells. The glandular epithelium itself shows granular degeneration, with more or less fatty change and atrophy, and the lumen contains debris, for the cells themselves have desquamated. Hyperemia occurs either diffusely or in patches, and there are more or less minute hemorrhages. Leukocytes have escaped from the surrounding dilated capillaries, and a certain amount of small-celled infiltration is evident in the interstitial tissue. The solitary lymph follicles may be swollen, and sometimes burst on to the surface, leaving minute ulcers. The resulting changes affect the secretion of mucus and gastric juice, and alter the general functions. Hence disturbances of the sensory, secretory, absorptive, and motor gastric functions occur.

Symptoms.—These depend much upon the cause. Usually within a few hours, or at most a couple of days after action of the causative agent, there is gastric discomfort, fulness and sense of pressure or pain, with pyrosis, nausea, and vomiting. Often an initial rigor or chilliness ushers in the disease. The patient complains of a curious taste, sometimes bitter; there is also salivation. Thirst is a prominent feature. Nausea usually precedes the vomiting and occurs with food or at the mere thought of it; vomiting itself occurs early and gives relief. The vomitus contains undigested food, mucus, bile, and sometimes streaks of blood. It is bitter in taste, and, as a rule, of a foul odor. Cardialgia, pyrosis, and waterbrash add to the distress. The teeth are set on edge and the burning acid fluid irritates the pharynx and œsophagus. There is hiccough, and eructations of gas, either bitter or tasteless, are common. Pain is almost always present, slight or severe, and sudden or gradual and progressive. With all these subjective sensations are numerous nervous phenomena, headache, dizziness, and depression of spirits.

Signs.—The patient shows more or less prostration, and, if the condition be at all severe, the face is pale, the extremities are cold, and he breaks out in a cold and clammy perspiration. The pulse is at first increased, later lessened in rapidity. Fever, if present, appears early, and is usually slight, although sometimes, when there is an initial chill, it may be high and accompanied by herpes; often, indeed, there is no fever throughout, but when, on the other hand, fever persists for days, one should examine carefully for some other factor to which gastritis may be merely secondary. In the so-called epidemic or infectious gastritis, the fever remains high for days, sometimes even for several weeks. The condition differs otherwise but little from ordinary simple gastritis, although an enteritis is more frequent and the general symptoms are more severe.

The tongue is coated, usually dry, and indented where the edges come in contact with the teeth. The breath is foul and salivation is marked. Herpes labialis is often present. The epigastrium shows distention and tenderness. The vomitus contains HCl with lactic and fatty acids, and mucus, and there is motor insufficiency of a mild degree. The test meal likewise shows evidence of stagnation and perhaps subacidity, while mucus is excessive. After a test breakfast the bread is almost unchanged, much mucus is present, and HCl is absent or much diminished. There is usually constipation or later on diarrhœa, and involvement of the intestines is an important and often troublesome

complication. Jaundice may be present if the common duct is obtsructed by a plug of mucus. The urine is scanty, high colored, has a high specific gravity, and shows abundance of urates.

Diagnosis.—The etiology is an important factor, while the acute onset and the reaction to treatment suffice to make the condition clear. The absence of a known and plausible cause should suggest caution in a diagnosis which may subsequently require modification. The differential diagnosis deals mainly with gastric neuroses, neuralgia, and hyperacidity, hysteria and ulcer. Further, biliary colic, catarrhal jaundice, appendicitis, incarcerated hernia, ileus, and the onset of some infectious disease, especially typhoid fever, scarlet fever, smallpox, and pneumonia have to be considered. The gastric crises of tabes dorsalis, the onset of menengitis in children, and lastly pregnancy should not be forgotten in considering the differential diagnosis, for awkward mistakes are thereby avoided. The appropriate adjustment of the history and symptoms to the physical findings usually make the diagnosis simple. *Exclusion of the important causes of a secondary gastritis* is the essential point.

Prognosis.—This depends on whether the condition be primary or secondary, and the gravity of the associated underlying cause. As a rule, primary acute simple gastritis quickly responds to appropriate treatment. The more frequent the attacks, however, the greater the liability to recurrence. The course and duration depend very largely on the cause and severity. The symptoms may last merely for twenty-four hours, or in severe cases for several weeks. Sometimes vomiting relieves at once, but such cases are in most instances merely acute dyspepsia, *i. e.*, acute disturbances of function. When the intestines are involved the disease is aggravated and its duration lengthened. Fatal cases are those in which the gastritis is secondary to some other disease, usually some severe infection or intoxication.

Treatment.—*Prophylaxis.*—In children the cause is more frequently dietetic than in the adult, and in them proper feeding is an importatu prophylactic measure. The overloading of children's stomachs with unsuitable food is a frequent cause of gastritis.

The Direct Treatment.—Two considerations are of special importance: (1) To remove the cause. (2) To protect the stomach and lessen the inflammation.

1. Nature often provides for the removal of the cause by inducing vomiting, and subsequently anorexia; or else emesis may be produced by some simple measures. The remnants often irritate and keep up the symptoms, and are liable to add intestinal disturbances, so that frequently it is well to wash out the stomach; this is especially useful with children because thorough and rapid in its effects. When vomiting is not rapidly induced one may use emetics with care, apomorphine hypodermically, or a mixture of tartar emetic, gr. $\frac{1}{4}$ (gm. 0.016), and pulv. ipecac, gr. 5 (gm. 0.3), every quarter of an hour until it acts. The latter drug is especially useful for children in the form of vin. ipecac. in ℥j doses. Other medicines are rarely required.

2. For twenty-four hours the stomach should be given as complete a rest as possible. A little ice relieves the thirst and a suitable mouth-

wash should be in frequent use. Whatever else is given should be in small quantities and only in fluid form, for example, a little weak, unsweetened tea, perhaps with brandy; effervescent water or soda lemonade; peppermint tea; later milk and lime-water (or soda-water) may be taken, other food being begun only when the desire for food returns. Pancreatized milk is also useful. Broths, gruel, and a little stale bread may be added. Solid food is given later on if no diarrhœa be present, the transition period being devoted to light puddings, rice, etc., then lean fish, and later on stewed chicken and fillet. Light vegetables should be allowed only after some days of convalescence when the stools are quite normal, for relapses are common and easily induced by too early a return to a mixed diet. Rectal feeding is rarely needed, but is advisable for those of advanced years.

Medicinal.—The early administration of muriatic acid is beneficial, sometimes in 8 to 10 drop doses of the dilute acid in a wineglass of water, taken in sips before meals, or else after food. Narcotics are not usually required, and may do harm by stopping peristalsis and thus prolonging the symptoms.

Mechanical Measures.—A Priessnitz compress and an early warm bath are sometimes of use.

Special Symptoms.—For the constipation, drastic purgatives are to be condemned; however, small doses of calomel and soda are useful, especially for infants, or castor oil and laudanum. "Fluid magnesia" is preferable in mild cases because less drastic. For the diarrhœa, lime-water in doses of a few ounces every two hours, or bismuth and chalk in powder form may be given. For the nausea and to rest the stomach, cocaine in doses of gr. $\frac{1}{4}$ (gm. 0.016), or creosote in 1 drop doses may benefit. Vomiting is best treated with rest, and the administration of dilute hydrocyanic acid in doses of 5 minims with bismuth, soda, and spirit of chloroform, although, as a rule, a sufficiently prolonged abstinence will in itself suffice.

Phlegmonous Gastritis.—Synonyms.—Interstitial purulent gastritis; inflammation of the submucosa (Rokitansky); gastritis submucosa (Dittrich, Klebs, and others); phlegmon ventriculi; linitis plastica et suppurativa (Brinton); linite phlegmoneuse.

Definition.—This is an acute suppurative inflammation of the gastric submucosa, sometimes primary, but usually secondary as a metastatic or other infection. It may be diffuse or circumscribed. In 1904, Robson and Moynihan collected 85 cases. Since then others have been described, and more than 100 cases are now on record.

Etiology.—The condition is rare, especially in its primary forms. The primary cases are doubtless all microbic in origin, although alcohol is often regarded as a predisposing factor. Marasmus, faulty diet and ptomaines, corrosive poisons, *e. g.*, oil of turpentine (Kelynack), oxalic acid and trauma of various kinds (Hopkins), all play a part. A fair proportion of cases follow gastro-enterostomy and other operations of the stomach. The commoner causes are some general infection, *e. g.*, scarlet fever, smallpox, typhoid, etc., an ulcerating cancer or infected ulcer, or some defect in the mucosa admitting virulent bacteria. In a number of the

cases hemorrhagic erosions suggested the site of invasion, or the infection may occur through the mucous membrane, even without the presence of a defect (Konstantinovitch). More rarely pus swallowed from a suppurative stomatitis has caused the disease. Streptococci have been the commonest microörganisms present, and the colon bacillus frequently coexists. Many other common bacteria have been found and sometimes yeast. The bacteriological examination is not always satisfactory, for coccus forms may die off early, leaving the field to other organisms not directly associated with the true cause.

Age.—The youngest patient afflicted was ten years of age (Hun), the eldest eighty-five. The diffuse lesions nearly all occurred between twenty and sixty years.

Sex.—The proportion is about four males to one female.

Pathology.—Of the 96 cases collected, 76 were probably of the diffuse variety and 12 were definitely circumscribed. The remaining cases recovered or did not come to autopsy. The disease commences in the submucosa, and unless a local ulceration (benign or malignant) exists, or some generalized infection, it is not always easy to determine the origin. Cases originating in chronic ulcer and in cancer are not uncommon. The submucosa, especially at the pylorus, is thickened, infiltrated with pus or sero-pus, sometimes almost jelly-like or œdematous in appearance. The underlying muscle is involved to a greater or less extent; indeed, it may be entirely destroyed. Sometimes merely a channel or cavity remains, containing little or no pus whatsoever. The mucosa is usually more or less affected and signs of infiltration are seen between the glandular loops.

The mucosa is thickened, hyperemic, and ecchymotic in patches. The epithelium is here and there degenerated, and erosions and ulcers are frequent. Sometimes the sinuses leading from the submucosa are so numerous as to give to the lining membrane a coarse or fine sieve-like appearance. The result may be that more or less of the mucosa is lifted away from the underlying submucous layer. The peritoneal surface may show marked swelling of the lymphatics. Perigastritis always accompanies the malady and adhesions occur in various ways and situations. Purulent peritonitis is not infrequent, or infiltration and dissection may occur along the submucosa of the duodenum or up into the œsophagus (Chvostek). The diaphragm has been invaded, resulting in a purulent pleurisy or pericarditis. Thrombi are often found in the neighboring veins and the causative microörganism is not infrequently detected in the vessels.

Splenic tumor, acute nephritis, necrosis of the colon, mediastinitis, cholecystitis, etc., may result from the primary gastric affection, or as a part of a general septic state. The circumscribed phlegmonous gastritis forms an abscess of varying size in the submucosa, or there may be numerous smaller collections. Perforation may occur into the stomach cavity, externally into the peritoneum or into neighboring viscera.

Symptoms.—*The Diffuse Variety.*—The onset is nearly always sudden, although with no characteristic symptoms. A rigor may usher in the affection, followed by a rise of temperature to 104° or 105° F. There is

general malaise, and severe prostration appears very early. Very soon the gastric symptoms become marked. Not infrequently two stages are evident, at first the signs of gastritis and later those of peritoneal inflammation. Some cases, however, show no gastric symptoms whatever, and the condition is found only after death.

Nausea and *vomiting* apppear early, are of long duration and rarely, absent. Toward the end the vomiting usually diminishes; it may be feculent and foul. The vomitus rarely contains macroscopic pus, unless the mucosa be perforated, although leukocytes are usually seen on microscopic examination of the gastric contents. Progressively increasing pain in the epigastrium is a prominent feature and rarely absent. Soon the pain extends over the whole gastric area, resembling that of local or general peritonitis. Tenderness is usually present, and if a large abscess exists fluctuation may be detected. Meteorism is often marked. The fever is irregular, usually persistent, and has a wide range; in Testi's case, however, there was no elevation of temperature. Repeated rigors are sometimes present. The pulse is rapid, small, and often irregular in volume and rhythm. There may be diarrhœa or constipation, and thirst is often marked. Collapse, which has been imminent from the onset, becomes progressive; delirium and coma usually usher in the final stage, with or without the signs of general peritonitis. The *course* is progressively downward and the duration is rarely longer than two weeks. The diffuse cases are more rapid than those which are circumscribed.

The *circumscribed variety* presents a similar type of symptoms, although at first less severe. Sometimes pain is quite absent. A distinct tumor is often felt. The abscess may burst into the peritoneal cavity and cause death, or rupture may occur through the mucosa into the stomach. Some of these cases recover as pathological specimens testify.

Diagnosis.—This has rarely been made. The signs are those of acute peritonitis (local or general). Leube has pointed out that the vomiting of pus need not be pathognomonic, and may arise from a purulent gastritis alone. The probable diagnosis is suggested when in the course of a pyemia or other severe general infection, the symptoms arise as above described, although this form of metastatic infection is comparatively rare. The circumscribed form is perhaps more readily diagnosed, especially when a tumor, which has already been felt, disappears after the vomiting of pus; though this may arise from an abscess arising outside of the stomach and perforating into the viscus. Leukocytosis is probably present in most of the cases (Lengeman). In the differential diagnosis one must consider chiefly perigastritis following ulcer, peritonitis, acute pancreatitis, cholecystitis, abscess of the liver, and corrosive poisoning.

Prognosis.—About 95 per cent. of the recorded cases have been fatal. Death usually occurs within one week, and many end fatally in two or three days. The more subacute and chronic cases later on develop peritonitis or metastases.

Treatment.—This is symptomatic, unless a localized abscess is diagnosed, in which case operation offers some hope of success. Mikulicz had a patient thus cured (Lengeman). Bovée described an undoubted phlegmonous gastritis cured by gastrostomy and drainage.

Severe Toxic Gastritis.—Various irritant and corrosive poisons when brought into contact with the gastric mucosa induce an intense inflammation which is merely an aggravated form of the acute simple gastritis, the intensity depending on the character of the poison, its nature, concentration, quantity, and length of time present in the stomach, as well as upon the volitional or accidental ingestion of the irritant. These cases are not necessarily severe, and all stages occur from simple hyperemia to ulceration, gangrene, and perforation. Practically all the known poisons may directly or indirectly induce a severe gastritis.

The *exogenous* poisons are especially irritant in their action, *i. e.*, concentrated acids, alkalis and alkaline salts (sodium and potassium salts, potassium and sodium hydrates, ammonia compounds, etc.), metalloids (chlorine, bromine, and iodine preparations, phosphorus, sulphur, arsenic, and antimony), metallic salts (lead, silver, zinc, copper, mercury, etc.), certain of the methane derivatives in large doses (alcohol, petroleum, croton oil, etc.), bodies from the aromatic groups in certain dosages (benzol and its derivatives), ethereal oils, turpentines, balsams; also some of the alkaloids and glucosides, etc.

The *endogenous* group includes poisons which are supposed to result from retention in the body of injurious substances which are under normal conditions eliminated by various channels, *e. g.*, in uremia and cholemia, and also poisons resulting directly from metabolic disturbances of a profound nature (diabetes, carcinoma, etc.). Further, there are the bacterial products from all forms of infections, almost any of which may directly or indirectly act as irritants to the gastric mucosa.

The action of the different poisons varies not only according to their nature, but likewise according to the method of ingestion and the position of the victim while taking the irritant. The site of the lesion varies. Sometimes but a small portion is affected; sometimes merely the cardia is involved; or, again, only the greater curvature. Most change naturally occurs where the poison was longest in contact with the wall, which event occurs in most instances at the fundus, pylorus, and posterior wall. As repair takes place, scars form, and according to the extent of the original lesion mere cicatrices exist, or else more or less deformity develops. As a result one may find pyloric stenosis, hour-glass contractions, sacculations, etc. Often very extensive lesions heal remarkably well. The mucous membrane is not impaired. The secretory changes are marked; hydrochloric acid diminishes or is completely absent.

As a rule, the alkalis are more penetrating than acids; perforation is extremely common, and where the serious effects are not fatal one usually finds more or less deformity of the œsophagus as the result of cicatricial contractions. Often the œsophagus alone is severely affected, for the acid becomes diluted in its journey to the stomach.

Symptoms.—In a typical case the sudden severe onset of pain and vomiting is the most prominent feature. The pain is usually felt all the way from the oral cavity to the stomach. There are burning pains in the mouth and gullet, and behind the sternum. Nausea, retching, and vomiting follow almost immediately. The vomiting is frequent, painful, and brings no relief of the symptoms. In the vomitus blood-stained

material, perhaps food remnants, mucus, shreds of mucous membrane and the poison itself are found. Great thirst is a prominent symptom, and the dysphagia intensifies the suffering. Diarrhœa appears later, and the stools may show evidences of mucus and blood, usually because of an accompanying enteritis. Signs of collapse rapidly supervene. The facies is anxious and pale, or cyanosed, and the lips and mouth show evidences of the corroding poison. Petechiæ often appear in the skin, and jaundice is not infrequently present from toxic or obstructive causes. The pulse is rapid, small, and often irregular in volume and rhythm. The respirations are shallow, quickened, and thoracic in type, because the diaphragmatic movements are limited through the pain. The temperature may rise slightly above the normal. The condition of the sensorium varies according to the exciting cause. In many instances there is great excitement, convulsions intervene, and, later on, coma.

The condition of the *urine* depends on the kind of poison ingested. The abdomen in the acute stages shows nothing beyond tenderness and distention, unless perforation and peritonitis have occurred with their usual signs. Death occurs usually from exhaustion, convulsions, suffocation, or from general intoxication. Should recovery take place, complete restoration of the tissues may occur in those cases where no marked corrosion of the gastric mucosa has been present, but this is only with the milder forms of irritant poisoning. In other cases the results are less favorable. Chronic indigestion supervenes from atrophy of the glands, or persisting gastritis with vomiting, progressive weakness, and emaciation. Sometimes ulcerations persist, or their healing results in the formation of stenoses and deformities.

Diagnosis.—This is based on the history, the nature of the symptoms, the oral and pharyngeal evidences of corrosion, etc., the odor of the breath in certain cases, the chemical analysis of the vomitus or of the washings from the stomach, and the analysis of the urine.

Prognosis.—This depends upon the special cause, the kind of poison, its amount in relation to its toxicity and irritant properties, the early emesis, and the possibility of early removal. Collapse and peritonitis are serious symptoms.

Treatment.—Rational therapeutics depend upon a recognition of the special toxic agent, for which the proper antidote can be given. In addition to this, one should attempt to get rid of the poison, if early recognized, by rapidly acting emetics, *e. g.*, apomorphine. Lavage should be used when it is improbable that extensive corrosion is present, and soothing remedies for the gastric mucosa may then be administered. For corrosive acids one may give mucilaginous and oily drinks or weak alkalis. For corrosive alkalis, vinegar and water, or citric acid are useful. Counterirritants externally may aid in giving relief, while medicinally one should use demulcents, opiates, bismuth, etc. Rectal feeding will be necessary for some days. Collapse must be checked, or treated by appropriate remedies.

Mycotic Gastritis.—Many of the commoner parasites are found in the stomach under normal or abnormal conditions, both bacteria and mould fungi, as well as yeasts, and while in many instances they are the direct

cause of changes in the gastric functions or anatomical conditions, at other times their presence seems to be rather accidental and unimportant. Inflammation of the gastric mucous membrane as a result of bacterial invasion through the blood or lymph streams is common enough. Whether or not bacteria which are ingested with the food can induce a true gastritis seems open to question. It would appear that the acid gastric juice retards the growth and development of bacteria, although moulds seem to resist the acid better than do the schizomycetes, which latter grow better when subacidity is present. The acidity, the stagnation, and the quality of food ingested are the factors which determine the growth or retardation of development of the various fungi in the stomach.

As a general rule, moulds and yeasts do but little harm in the stomach and have an anatomical rather than a clinical interest and importance. Kundrat found favus in the stomach associated with a favus universalis, which was distributed throughout the body, and Rudnew found the penicillium glaucum in a woman who died of Asiatic cholera. Klebs and Fraenkel associated a gastritis with favus, yeast, and oidium albicans; certainly the last-named fungus has often been seen in cases of gastritis, and yet in spite of its frequency during childhood in the pharynx and œsophagus, it is rare in the stomach. Epstein drew attention to the fact that a healthy mucosa was not a suitable medium for the growth of this parasite in the pharynx, and perhaps the same applies to its growth in the stomach. This may account for the frequently abrupt termination of the affection at the cardia, despite the fact that large numbers of the fungi reach the interior of the stomach.

Von Wahl and von Recklinghausen recorded cases in which fungi of the leptothrix group penetrated the gland ducts and were anatomically associated with necrotic areas. In one case many pustules existed in the glandular layer and submucosa of the pylorus, in the other the fundus was chiefly involved.

Symptoms.—The relation of the presence of moulds to the symptoms is dubious. Talma was of the opinion that the carbohydrate fermentation, caused by the presence of microörganisms, was the antecedent of many cases of hyperacidity, but although moulds may coexist with hyperacidity and gastralgia, it is not certain whether their presence is cause or effect. The lavage water from the empty stomach shows the presence of blackish-gray or brownish-green flakes indicating the existence of moulds which microscopically showed spores and mycelia. These flakes varied in number from 4 to 50 or more, were 2 to 5 mm. in size, and often intimately mixed with mucus, which fact together with their presence in the empty stomach argues that their presence is not merely an accidental admixture. Probably the moulds adhered closely to the mucous membrane and perhaps proliferated in it. They can evidently thrive in the stomach and retain their power of growth, regardless of the gastric juice.

Two types of cases occur, one with signs of hyperchlorhydria (occasionally with hypersecretion and vomiting), the other with gastralgia, the gastric secretion being normal or reduced. The relation of the fungi to the symptoms is either etiological or a cause of increased severity.

Treatment.—Systematic lavage rapidly removes the fungi permanently from the stomach. Einhorn advised the further use of weak solutions of silver nitrate in the lavage water.

Diphtheritic Gastritis (Gastritis Membranacea).—This condition, which has much more anatomical than clinical significance, may be defined as a pseudomembranous inflammation of the gastric mucosa, usually a sequel to a similar condition of the nasopharynx, but sometimes primary (Delafield) and associated with varying bacterial agents, and at other times apparently due chiefly to chemical causes.

True *diphtheria* of the stomach, due to the diphtheria bacillus, is rare and nearly always secondary to a similar bacterial invasion of the contiguous parts, œsophagus, throat, or upper respiratory passages. Leary observed only 2 instances out of 136 fatal diphtheria cases at the Boston City Hospital. While, as a rule, diphtheritic gastritis is secondary to some other diphtherial infection, it may complicate various other infectious diseases, *e. g.*, typhoid fever (Thorel), pneumonia (Foulerton), pyemia, the exanthemata, etc. Children seem to be most commonly affected.

Pathology.—The stomach is not usually altered in size or shape. The chief feature is the presence of the pseudomembrane. This may be diffuse and cover the entire surface of the stomach but more often there are irregular streaks or patches of membrane—of varying size, thickness, and number. The mucosa is discolored, usually darker than normal, reddish or grayish red in appearance, and thickened. The rugæ are usually well-marked, and covered with the more or less firmly adherent membrane. Microscopically the picture resembles that seen in ordinary pseudomembranous lesions of any mucous membrane. Streptococci and diphtheria bacilli are most commonly isolated.

Symptoms.—There are no characteristic symptoms, and the mere vomiting of a pseudomembrane does not necessarily imply that the disease has affected the stomach itself—unless, indeed, a cast of the whole stomach be vomited, as was recorded by Thomson in one instance. Such membranes are readily swallowed and sometimes are so extensive as to cause pyloric obstruction. Seitz has recorded a diagnosis of pseudomembranous gastritis during life and confirmed at autopsy. Some of the membrane has been vomited concurrently with the presence of other evidences of gastric disturbance.

CHRONIC GASTRITIS

Definition.—A protracted inflammation of the gastric mucous membrane with motor or secretory changes in gastric digestion. It may be primary or secondary.

Incidence.—In its primary pure form the condition is clinically quite uncommon—at all events much more rare than is ordinarily supposed—being frequently confused with a purely functional disease in which similar signs and symptoms exist without any pathological changes. For this reason, and in view of the unsatisfactory means of diagnosis, the time-honored term "chronic dyspepsia" should not be despised. It

may be that after some time even functional disturbances lead to pathological changes in the gastric mucous membrane, a true superficial inflammation, as in the cases referred to by Cohnheim, in which the gastritis resulted in his opinion from motor insufficiency, and was induced by irritation of the stagnant chyme.

As a primary affection, chronic gastritis is not often found in the autopsy room, the cause of death usually being some general or local condition to which the gastritis is secondary (cardiac or hepatic disease, nephritis, tuberculosis, pernicious anemia, etc.). Thus, in the Royal Victoria Hospital, among 1300 autopsies, there were 108 with chronic gastritis, and of these, 92 were definitely secondary to other causes, while the remaining 16 were more or less mild in type and associated with other diseases not necessarily the cause of the condition. Statistics, however, with reference to the incidence of chronic gastritis are notoriously unreliable. *Clinically*, the signs and symptoms are often most ill-defined as evidence of true inflammation of the stomach, and much has been called gastritis which undoubtedly would more truly come under the category of neurosis of the stomach, or under the old name of chronic dyspepsia, a purely functional disorder often due to atony. *Vice versa*, many cases of chronic gastritis at autopsy (secondary to other diseases) were utterly devoid of evidence of that malady during life.

Pathologically, statistics are almost equally unreliable, through the infrequency with which primary gastritis comes to the pathologist's notice, and because of the numerous errors in pathological observations. Marked contractions of the gastric wall are mistaken for chronic thickening, and passive congestion for true gastritis, where a microscopic examination would have revealed no sign of disease.

Classification.—Classifications have been based upon the nature of secretions, and the gastritis acida, gastritis anacida, gastritis mucosa, etc., have been described. The mere analysis of the secretions, however, affords practically little clue to the underlying conditions, and cannot determine differentiation from certain neuroses. In many instances a hyperacid secretion is found in the early stages of chronic gastritis to be followed later by a diminution of the hydrochloric acid. Sometimes, however, hyperacidity may appear late, while not infrequently it persists throughout the whole course. When one realizes how widely the secretions may vary from day to day; how on one day an excessive acidity may be followed by a marked hypochlorhydria on the next; how intermittent is the pathological secretion of mucus, one can scarcely feel safe in relying upon a classification of chronic gastritis based on such clinical signs. As well might one classify the various forms of pneumonia according to the account and character of the sputum.

The term *mucous gastritis*, for example, is used to designate the simple chronic gastritis, or gastric catarrh, in spite of the fact that mucus may be abundant in any of the different pathological varieties of this malady. Again, in hyperacid gastritis much or little mucus may be present, and the underlying condition may be proliferative and degenerative in nature. Proliferative gastritis, as a rule, induces diminution in the secretion of HCl, although, in many instances, there is hyperacidity.

In cases of chronic gastritis with atrophy of the glands (anadenia, achylia gastrica), the symptoms and signs are apt to be most constant; in certain instances of this variety there is a rapid course with signs of chronic gastritis and progressively downward tendency. Examination of the gastric contents after a test meal shows little or no digestion and the secretions appear absent. Here, however, as in the other forms of chronic gastritis, great variations occur in the symptoms at times, and, moreover, there are all grades of transition to the other varieties of the disease. Again, whether owing to treatment or to the natural course of the malady, a hyperacid gastritis may change to the anacid type, and, *vice versa*; if enough gland elements remain, the condition of achylia gastrica may alter to one with normal or even hyperacid secretion.

Apparently the state of the *motor* power has greater significance in the production of clinical signs and symptoms than has the secretory function; often indeed the marked evidences of the malady are synchronous with the signs of motor insufficiency. Certainly many cases in which autopsy has shown marked disease of the gastric mucosa have given few symptoms during life so long as the motor power was unimpaired. It would seem well, therefore, to avoid any clinical classification into subdivisions, and to recognize the fact that the manifestations being varied, one may recognize the malady from the complexity of signs, symptoms, etiological factors, and be content with the general diagnosis in all such cases of "chronic gastritis."

Etiology.—Primary chronic gastritis is mainly caused by irritants acting over a prolonged period and in a strength not so great as to corrode the mucosa. Oft-recurring acute gastritis is followed by the chronic form. *Alcohol* is the commonest irritant, and the most important cause, especially if taken undiluted, *e. g.*, brandy, gin, or wines of all kinds when taken to excess—their action being either as direct irritants or perhaps in part due to the production of acids in the stomach. So also diluted alcohol may act in the same way by inducing acetic fermentation.

An analysis of cases in the Royal Victoria Hospital has called our attention to the fact that alcohol in excess is by no means a necessary cause. In 10 autopsies performed on men dead of acute alcoholism, 7 showed no definite chronic gastritis whatever, while in the others the signs were marked in only one. Of the autopsies upon 40 other patients, in whom a marked alcoholic history was obtained, but in whom death was due to other causes, there were 20 cases with chronic gastritis, and the remainder showed no definite signs of true inflammation; 10 showed mere congestion, 10 showed swelling and congestion, 9 showed a granular mucosa, and only 5 showed definite thickening; 4 others had mammillations, and in the remaining 2 true polypi existed. Macroscopic erosions existed in only 1 of these 40 cases. It is interesting to note that 21 of these 40 patients gave no history of gastric symptoms, while 16 had pain and vomiting.

Other causes of irritation acting directly or indirectly are spices, strong tea or coffee, certain irritant drugs and drastic purgatives, as also tobacco, especially if chewed, and dietetic errors, Improper quality of food (if coarse, too rich, too spicy, fatty, or otherwise irritating), excessive

quantity as regards bulk, especially of rich foods, improper mastication of food and also irregularity at meals are all of great importance, and more so in proportion as the individual's habits are sedentary.

Secondary gastritis may be due to local or general conditions. The chief local conditions are as follows: Gastric diseases of any chronic nature, affections of the portal system, especially obstruction, and also the presence of parasites (bothriocephalus, etc.). The main general conditions are numerous, *e. g.*, cardiac and arterial disease, pernicious anemia, leukemia, gout, diabetes, etc., and general infections (typhoid fever, pneumonia, tuberculosis, sepsis, etc.).

Pathology.—Pathologically two main types of chronic gastritis exist, the one *chronic productive*, the other *atrophic*. In the productive type, part or all of the stomach wall is thickened, while in the atrophic variety it is thinned in one or all of its coats. The stomach is usually larger than normal, except in the cirrhotic forms where there is shrinkage of the organ. At autopsy, mucus is usually thick, or a more or less grayish or slaty color, and sometimes reddened with blood pigment. It is either translucent or opaque, and sometimes appears semipurulent.

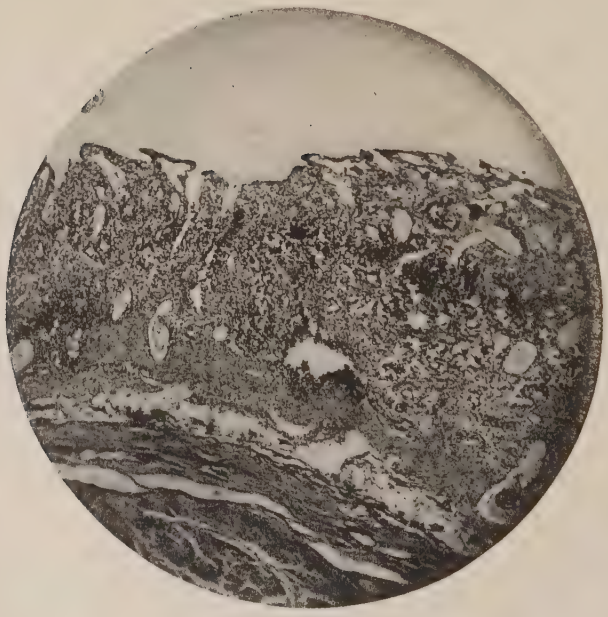
The mucous membrane varies according to the type of gastritis present, but both types may be found in different portions of the same stomach. In the *productive variety* the mucosa is swollen and thickened, and of a dark red or grayish-red color, especially in the neighborhood of the pylorus. The color varies. In the older cases there is more pigment, which appears beneath the mucosa as a black or dark gray discrete discoloration. Not infrequently one sees small, follicular ulcers or hemorrhagic erosions, apparently due to inflammatory hyperplasia of the lymph follicles, with subsequent degeneration. The affection of the mucosa is either general or local. In diffuse inflammation there is dense thickening from interglandular inflammation as well as from productive inflammation of the gland structures. The thickened wrinkled mucosa with its flat mammillated appearance may be polypoid in appearance ("gastritis polyposa") or more coarsely granular (gastritis granulosa). The submucosa and muscularis may also be affected, the muscle itself thickened, and the interstitial tissue increased. One may even see the serosa involved.

Microscopically, the mucous membrane shows small-celled infiltration, degenerated epithelium, hemorrhages, cystic dilatation of the gland tubules, and here and there some true erosions. The round-celled infiltration occurs early, is usually chiefly superficial and beneath the uppermost layers of epithelium, as also to some extent between the glands. Small round-celled infiltration may persist for a long period of time without developing into fibrosis. The degeneration of epithelium affects mainly the secreting cells, while the mucous cells appear to resist the inflammation longest. Often the epithelium is so distorted that it is impossible to distinguish chief from parietal cells, and many assume a cylindrical or a cuboidal shape. Cystic dilatation of the tubules is common (retention cysts). This so-called "gastritis cystica" is sometimes very pronounced. Capillaries and lymphatics are usually dilated and there are hemorrhages, old and new.

FIG. 37

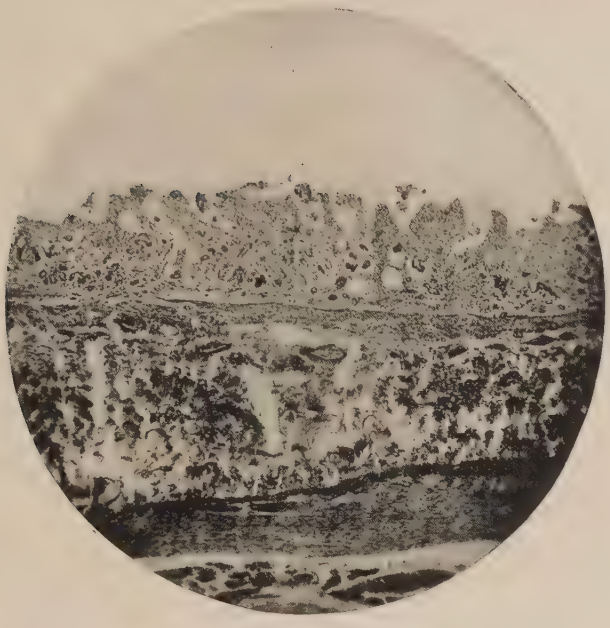
Chronic productive gastritis.

FIG. 38



Chronic productive gastritis.

FIG. 39



Chronic productive gastritis.

FIG. 40

Chronic productive gastritis.

Atrophic Type.—The second type of chronic gastritis, with atrophy of the mucous membrane, sometimes called *anadenia ventriculi*, is said to be preceded usually by gastritis proliferans. The mucous membrane is devoid of properly developed glands. The surface is pale, thin, and smooth and in the advanced cases consists more of granulation tissue or well-developed fibrous tissue. The muscularis takes part in the process and is usually atrophic. Sometimes, however, there is muscular hypertrophy with atrophy of the mucosa, and one may see pigmentary changes, the so-called atrophic pigment induration.

Microscopically, the mucosa resembles more and more that of the small intestine. There are evidences of round-celled infiltration. The atrophy of gland structures varies; often the secreting glands are alone involved, while the mucoid cells are unaffected; but the changes in this respect vary in different cases, as well as in different portions of the stomach in each individual instance. Illustrative types of these cases are often found in pernicious anemia. Some advanced cases are difficult to distinguish from a diffuse scirrhus, the gland structures being so atrophied that only a flat fibroid-looking surface remains whose base enclosed the remains of gland structures.

Cirrhosis of the stomach is only another variety of the atrophic in the sense that gland structures disappear. Here the organ is smaller than normal, contracted, and thickened usually in all its coats from excessive growth of the products of chronic inflammation.

Symptoms.—The disease both in its primary and secondary forms, may be latent throughout, or gradual and insidious in onset. To a certain extent the symptoms and signs depend upon the condition of the secretions and motor power, although certain general features apply to most of the cases.

Early symptoms are usually those of a so-called dyspepsia; slight dietetic errors cause discomfort in the epigastrium, with a sense of fulness, pressure, or weight, and perhaps even slight pain. Unless hyperacidity exists there is usually anorexia, especially for meats, or the appetite is fickle, with yearning for spices, acids, or liquids. A disagreeable taste in the mouth is present, and flatulence commonly intervenes, often being a marked symptom. Eructations of gas frequently relieve the distress. The tongue may be furred and is often sore at the edges and tip. Nausea and vomiting occur either at the height of digestion or sometimes in the early morning—perhaps induced by the swallowing of pharyngeal mucus during the sleep. Thirst is usually present, although less common than in acute cases. Lassitude, neurasthenia, and dizziness during the digestive period are the rule. Later in the disease, when the condition is more pronounced the symptoms are aggravated. Nausea is more persistent, waterbrash and cardialgia are more common, and vomiting comes on with greater frequency and the vomitus contains undigested food with fermentation products. Fluids may be well borne, but solids aggravate the symptoms. The *intestines* are likewise affected, and constipation alternates with diarrhœa. The *nutrition* varies. Emaciation may be rapid when the intestinal functions are simultaneously

impaired. The urine shows urates and calcium oxalate is often present in excess. Not infrequently the ethereal sulphates are increased.

Physical examination of the abdomen gives little information, as the only constant sign is tenderness—more or less diffuse and perhaps more often found to the right of the epigastrium than elsewhere. The stomach may or may not be distended.

Gastric Contents.—Usually the food removed is abnormally large in amount, appears undigested, coarse, and mixed with mucus. The most constant abnormality is the excessive amount of *mucus*, although it may originate in some portion of the tract above the stomach, *e. g.*, pharynx or œsophagus, and need not be an evidence of disturbed gastric function. Mucus from the stomach occurs more commonly in shreds or flakes, not in isolated lumps, is mixed with the food and is often found in most abundance after the test meal has been removed and the remaining contents gained by thorough lavage. It usually contains leukocytes in more or less abundance. The presence of abundant gastric mucus enclosing many leukocytes is positive evidence of gastric catarrh.

The secretion of acid varies. Best and Cohnheim showed that in gastritis we first have subacidity through deficient secretory function and the neutralizing effect of alkaline mucus. The gastric juice is thus too weak to exercise its inhibitory acid action, so that the stomach empties itself too quickly and as a result we again get hyperacidity with its characteristic symptoms. They produced hyperacidity in dogs by artificially emptying the stomach more quickly, *e. g.*, by a fistula, thus doing away with the acid which regulates the movements. *Hyperacidity* is uncommon and when present usually indicates an early condition of the gastritis, or an associated neurosis (gastritis acida) Diminution of hydrochloric acid is more common and may be progressive up to the period of total achylia (achylia gastrica, atrophic gastritis). From time to time, however, during the course the amount of acid shows great variation. McCaskey, in an analysis of 600 cases of so-called chronic gastritis, found no hydrochloric acid in 20 per cent., subacidity in 26 per cent, normal acidity in 34 per cent., and hyperacidity in 20 per cent.

The *pepsin* keeps pace with the hydrochloric acid, and the *rennet ferment* likewise diminishes with the progress of the disease. Bouveret regards a quantitative estimation of the rennet ferment as a valuable aid in prognosis as indicating possibilities of repair.

Achylia not infrequently occurs in the late stages of chronic gastritis. From the pathological standpoint achylia does not imply anadenia. Faber, especially, draws attention to the fact that in gastritis there may be achylia even although secreting cells are unimpaired, and concludes that the accompanying gastritis has merely disturbed their function but not their structure. In order to prove that the achylia is not merely temporary, several test meals should be given. The enzymes are absent as well as the HCl; mucus may be abundant.

The motor power varies. As a rule it is not greatly impaired, although with insufficiency there is much more fermentation and the general gastric symptoms are more pronounced. In most cases of typical chronic

gastritis there is some atony, more readily induced by persistent dietetic errors. The gastric functions are taken on by the intestines when normal motor power exists. Gastrectasis is uncommon.

Some authors describe valuable aid from examination of bits of *mucous membrane* which sometimes come away with the lavage water, but there are many sources of error in this means of diagnosis. The alterations present are often but semblances of inflammatory change; and *vice versa*, even if the cells and glands be actually altered structurally, it does not necessarily mean that they have been functionally inactive. Bassler directed attention to the value of free gastric cells in the fasting stomach as evidence of the atrophic variety. Saline instillations are used (250 cc. of water with sodium chloride 21 grs., sodium sulphate, sodium carbonate and sodium phosphate āā 1 grain). The fluid is drunk, the stomach agitated by palpation and exercise, and after five minutes the fluid is siphoned off and allowed to stand. The sediment is then examined and the cells are differentiated by eosin (for acid cells), and hematoxylin (for peptic cells). In atrophic gastritis the acid cells are in abundance and stain readily, with stippled protoplasm and eosinophile granules with well defined nucleus.

Course and Prognosis.—It is usually of long duration, and the general health suffers either periodically or progressively, but alternation of good and depressed health is the rule. The mental condition suffers, neuroses appear and often great physical depression as a result of the hypochondriasis and neurasthenia. The exacerbations usually depend on indiscretions, and recurrences are very common, especially in alcoholics. The mild cases are readily cured, but in the more severe ones the probability of cure depends on the condition of the muscular wall, the state of the mucosa, and the kind and degree of inflammation present. With atony of the stomach, and especially gastrectasis, and with achylia gastrica, the condition is much more difficult to treat successfully. When the intestines are healthy, the chances of cure are naturally augmented. The prognosis should be based less upon the general condition than upon the outlook for securing a sufficient supply of nourishing food and the maintenance of secretory and motor functions. In every case the individual affected has himself most to do with the cure by observing due regard to the requirements of treatment.

Diagnosis.—The condition whether primary or secondary is very often latent, and repeated observations may be necessary; the etiology, the symptoms and signs as above described render the diagnosis certain, but by *exclusion* rather than by any other means. The main features in the diagnosis are: (1) The etiological factors. (2) Persistent indigestion, with nausea and frequent vomiting of much mucus, gastric pain, and tenderness. (3) The relation of the symptoms to the ingestion of food. (4) The variations in the course, with its exacerbations and remissions. (5) The moderate loss of strength and weight as compared to the lowered nutrition in more serious conditions. (6) The comparatively slight alterations of the motor power. (7) The presence in the gastric secretions of much mucus and variable quantities of acid from complete achylia to hyperacidity. (8) The finding in the stomach

contents of many leukocytes either in the mucus or in bits of mucous membrane. (9) The beneficial effect of proper treatment.

In the *differential diagnosis* one must distinguish between primary and secondary forms; the primary affection is much more uncommon than the secondary, hence the importance of detecting the original cause.

Chronic Gastritis and Gastric Neuroses.—The differentiation is often impossible. The distinctive features are as follows: In chronic gastritis, (1) An obvious cause. (2) Poor nutrition. (3) The symptoms are digestive in time and cause—much mucus is vomited. (4) Gastric analysis. (5) Duration with exacerbations and remissions.

In *cancer* there is no apparent cause, the disease is progressive with wasting, gastric pain, and hematemesis. The gastric analysis differs. There is occult blood in the stools, and tumor may ultimately appear. Treatment has less marked benefit. Atrophy of the gastric follicles, *achylia gastrica*, is an occasional sequel of chronic gastritis, as also an accompaniment of gastric cancer, pernicious anemia, etc. It may, however, occur as a neurosis. For years there may be complete absence of hydrochloric acid in the gastric secretions in individuals who are either well or merely neurotic. These patients show no dyspeptic signs in spite of the secretory deficiency, and show a mucosa which is perfectly normal according to observations made upon bits of mucosa removed in washings. In many instances even after years of achylia the secretions may return to the normal. The presence of much mucus and many leukocytes in the gastric contents in cases of achylia would seem to favor the diagnosis of gastritis, implying, as it does, a probable catarrh.

Treatment.—A detailed diagnosis is essential to the proper treatment of chronic gastritis. *Secondary* gastritis must be treated according to the cause, which will involve the therapeutics of the lungs, heart, liver, or general constitution. In the *primary* cases, on the other hand, the treatment embraces prophylaxis, palliative, and curative measures. The curative measures are mechanical, dietetic, and medicinal. One must consider the cause of the disease as well as the condition of the secretory and motor functions.

Prophylaxis.—This is of importance, and one should, therefore, remove any external conditions which tend to bring on or aggravate the malady. Excesses of all kinds must be guarded against; bad habits cured; the patient should be taught to eat slowly, to chew his food well, and carefully to select his diet both as regards quantity and quality. Faulty teeth, an important factor in the etiology of gastritis, should be repaired.

The *mechanical treatment* consists mainly in lavage, and is to be used only when atony and fermentation exist. It is well to clean the stomach before any food enters, to remove any mucus which covers up the superficial epithelium, and prevents proper action of the digestive juices. Lavage may be carried out daily or every second day, in the early morning, or, in severe cases, six hours after dinner (which is usually taken at midday), and the evening meal should be as light as possible. Lukewarm water usually suffices, but if much mucus is present, sodium chloride may be added, or, if there be much fermentation, boracic acid. The lavage water must return clear before the treatment is completed.

When, for one reason or another, lavage is impossible, one may employ "natural lavage" by means of frequent administration of mineral waters, especially the saline waters with carbonic acid, which are often beneficial in relieving the stomach of its mucus and inducing a combination of the organic acids. The alkaline sulphates (Carlsbad) are useful for this purpose as well as for relieving constipation. When there is irritation in the stomach with diarrhœa, they are best taken hot. Whenever atony exists only small quantities of fluid should be taken at one time.

Daily cold baths or shower baths, with subsequent friction of the skin, are of great benefit. When pain or great discomfort is present, a wet compress may be placed upon the epigastric area and covered with gutta-percha tissue. A suitable abdominal binder of thin wool is often soothing and is a protection to the sensitive abdomen. Electricity is of doubtful value, but the proper regulation of rest and exercise (which latter should always be moderate) is of the greatest importance.

A change of scene, climate, and general surroundings is one of the most efficacious forms of treatment, both for its stimulating effect on the constitution generally, and more particularly as an aid in dispelling the accompanying neurasthenia. A sojourn at some of the numerous watering places is often of the greatest benefit, not so much on account of the waters taken (although they have their definite use), but on account of the diet and general regime under which patients are placed, and under conditions which are not usually followed at home. When this is impossible, suitable exercise and properly regulated diversion are commendable, especially if accompanied by the regular use of mineral waters selected according to the condition of the secretions.

Dietetic treatment is of prime importance, although often hard to regulate because of the individual preference. The food must be non-irritating and easily digested, calling for little effort on the part of the gastric juice or muscular action of the organ. When only the scantiest diet is tolerated, milk, preferably diluted with lime-water, may be given at regular intervals, and this, while the patient is at rest, may suffice. Later on a mixed diet, selected with reference to the needs of each case, is advisable. The motor power is the best guide and when this of the stomach is normal, one may administer albumins, starches, and fats. When, again, the secretory power of the stomach is defective, a mixed diet is very easily given, so long as the motor power remains unimpaired. In all cases, however, albuminous food should be finely divided. Carbohydrates should form the bulk of the food in those cases in which the hydrochloric acid is deficient, using preferably those in which there is least residue after digestion is complete.

Fats are imperative when malnutrition exists, and for these cases butter and cream form the most easily digested varieties. It is thus essential, when possible, to give a mixed diet, non-irritating, finely divided, and containing as much nutriment as possible within the smallest compass. In severe cases, in addition to the milk, one may give gruel, milk soups, light puddings, rice, arrowroot, toast, and then eggs. In some cases minced meats may be added; but it is not wise to add spices or any rich sauce. The craving which many patients with a chronic

gastritis have for spicy things, under the impression that they will stimulate the functions of secretion, should not be encouraged. Of the lighter meats, calves' brains, sweetbreads, chicken, fish, minced beef, are best. Alcohol is to be avoided unless in the form of very light wine. The quantity of water taken with the meals should be restricted, unless there be hyperacidity, in which case it is well to dilute the food moderately. Effervescing alkaline waters may be tried with benefit.

The determination of the proper number of meals per day is based upon the condition of the motor power. If this be good, three meals a day may suffice, but if there be atony, four or five meals, each small in quantity, are better. Weak coffee, tea, and cocoa may be given except in hyperacidity. As the patient improves, such vegetables as spinach, carrots, maize, potatoes (mashed), and macaroni may be added in small quantities and gradually. Bread should be stale and not hot. When constipation is marked, it may be well to give stewed fruits.

Medicinal.—Inasmuch as hydrochloric acid is deficient in many cases, one may add a few drops after each meal with benefit. Thirty drops of dilute hydrochloric acid in a glass of water, to be sipped at intervals for an hour after each meal, may be prescribed. On the scientific basis, there is little to be gained from the use of pepsin, although practically one frequently does find that its employment seems to afford considerable aid to digestion. Pancreatin in doses of fifteen grains is perhaps better, and should be administered with soda, although rationally this should not be prescribed unless there is some evidence of atrophy of the gastric follicles. Papain is also recommended by many. After all, these artificially prepared ferments are realized to be of little use when one considers that the intestines carry on the defective actions of the stomach.

It seems of prime importance, however, to give some stomachic before each meal, and for this purpose one may try either dilute nitromuriatic acid, in doses of ♏x to xv (1 cc.), nux vomica, quassia, gentian, or condurango. In many cases the greatest relief from the pain is a pill consisting of silver nitrate, gr. $\frac{1}{6}$ (gm. 0.01); opium, gr. $\frac{1}{4}$ (gm. 0.016), and extract of hyoscyamus, gr. $\frac{1}{2}$ (gm. 0.03).

When fermentation is an annoyance the diet should be carefully looked into; one may sometimes add thymol, carbolic acid, or creosote. Germain Sée recommended strontium bromide, gr. 30 to 60 (gm. 2 to 4), especially when hyperacidity coexists. For a distinct pyrosis, bismuth subnitrate and sodium bicarbonate, of each 10 grains (gm. 0.6), combined with 3 to 5 grains (gm. 0.2 to 0.3) of calcined magnesia, will usually afford relief. Small doses of atropine may be added with benefit if the secretion of mucus is excessive. For persistent vomiting, lavage is the most rapid means of giving relief.

Constipation is one of the greatest annoyances. It is well that the patient should develop great regularity in his habits, going daily to stool at regular hours, whether there be any desire or not. As soon as possible vegetables containing much cellulose should be added to his food, also stewed fruits, especially a combination of figs and prunes; or in the early morning he should drink cold water or eat a fresh orange; and only in aggravated cases should we resort to either purgatives or

enemata. When purgation is necessary, it is a difficult matter to determine what drugs should be employed; only the mildest forms of purgatives should be given, and of these aloes and cascara are probably the most beneficial. The use of Carlsbad salts in the morning is efficacious also.

MOTOR INSUFFICIENCY

Synonym.—Gastrectasis.

Definition.—Gastrectasis is an acute or chronic enlargement of the stomach cavity associated with a relative or absolute diminution of motor power. The condition may be mild (mere atony) or severe (retention) and all transitions may occur. It is a clinical sign rather than a disease *per se*. In the severe variety there is permanent stagnation, *i. e.*, retention. It is a functional disturbance of motor power rather than mere enlargement of the organ. Of the functions of the stomach the motor is by far the most important, and modern methods of investigation confirm this view more and more.

The size and motor power of the stomach are not necessarily correlated. It is an organ whose size is subject to very wide variations in health, and clinical experience and *x*-rays prove the fact that mere increase in its dimensions does not imply a pathological state of the gastric functions. The stomach may occupy almost twice its normal area in the abdomen, without disturbance of its motor function. This is mere megalogastria, a matter of size and not of function.

Various forms of motor insufficiency exist: (1) Mere atony of mild degree (the commonest form of dyspepsia). (2) Severe atony (idiopathic dilatation), in which food is retained for a long time. (3) Relative motor insufficiency (obstructive), in which some hindrance at the pylorus, either intragastric (often hypertonic) or extragastric, causes the dilatation. These forms have in common one clinical sign, stagnation of food—other signs and symptoms depend on the severity and associated conditions. Probably the commonest form of gastric indigestion is that due to deficient muscular power—the so-called atonic dyspepsia—a condition of "slight motor insufficiency."

Atony without obstruction is not always easy to explain. Here again confusion seems to exist in the terminology. The motor power depends on rhythmical contractions of the antrum and action of the pyloric sphincter. The fundus plays a subordinate part, though recently an effort has been made to reëstablish its importance. Idiopathic dilatation seems to be quite easily induced. Cannon has shown that intragastric pressure has a marked influence on motility and that some mechanical stretching of the viscus is an efficient stimulus to muscular contraction. No smooth muscle can contract, however, until it has tone, *i. e.*, it must be shortened and resilient, ready for contraction when the stimulus comes. Without tonicity we get no rhythmical movements.

The *nervous system* plays an important part. The normal motor power depends upon the harmonious working of the two sets of nervous systems, vagal and sympathetic. The reflexes governing the motor power come through the stomach, the duodenum and jejunum, as

also, through psychic causes, and all sorts of reflexes may arise from the whole sensory periphery (*e. g.*, appetite, exercise, etc.). Tone for example is absent in general weakness of the body, as well as that of the nervous system, and without tone we get hypomotility. The propulsion of food is governed partly by the amount and character of the gastric secretion. Normally the passage of food is controlled by the duodenal mucous membrane, in other words, only as much food is passed through as can be utilized by the alkaline juices; if no acid exists we may get hypermotility because there is no acid to be utilized, *i. e.*, hypoacidity induces hypermotility, and *vice versa*, hyperacidity and hypersecretion may induce stagnation either from atony or from pyloric spasm, the latter induced by the irritation.

Cannon has shown that the rhythmic movements of the antrum are regulated by the action of HCl and it is the acid which keeps the cardia closed. The secretory values depend so much on motility that our methods of estimating increased HCl seem nowadays rather inaccurate. The normal gastric juice with atony may give hyperacidity to our tests, while if hypertonus exists a diminished HCl may be apparent.

Certain *mechanical factors* influence motility. (1) The amount of food in the stomach and (2) its consistence. The more food in the stomach, the quicker is this motility due to the distention (within limits), which acts as a stimulus to contraction. The fundus contractions are greater, the peristalsis of the pylorus is more energetic, and the intervals between the contractions are shorter.

All grades of motor insufficiency occur from mere atony to extreme gastrectasis, although whether these may be etiologically linked together is uncertain. Two conditions must exist to establish a rational use of the term gastrectasis—there must be enlargement of the organ and impairment of its motor power. The impairment may be merely relative, that is, the muscular activity may be greater than is normal, as when a pyloric stenosis hinders the rapid outflow. This terminology applies, however, only to the chronic forms, for the acute variety of dilatation is essentially a different condition and to be considered separately.

Acute Dilatation of the Stomach.—This is probably more common than is generally supposed, and certainly as a terminal feature in pneumonia and cardiac disease, as well as a complication in surgical conditions, it is by no means rare. German students have been described by Riedel as commonly affected after beer-drinking bouts, and it has followed other errors and indiscretions in the diet. Brinton referred to the condition in 1858 although Fagge first gave prominence to its clinical features. He recorded two fatal cases in patients eighteen and thirty years of age, in whom the stomach filled up rapidly with fluid. His description holds good today as one of the most complete pictures of the condition. Campbell Thompson, in 1902, collected 44 cases, and Neck, in 1906, recorded 60 instances. Conner[1] analyzed 102 cases of the disease (1907), and Laffer collected 217 cases in all.

Etiology.—Various degrees of dilatation occur involving the stomach alone, the stomach with the duodenum, the stomach with the duodenum

[1] *Am. Jour. Med. Sci.*, 1907, **133**, 345.

and jejunum, or the stomach with even a larger area of small intestine. This indicates that the causes must be varied and the pathogenesis different in various instances. There are predisposing and exciting causes, although it is not easy to dissociate these in all cases, all the more so as the etiology is apparently not only varied but often not to be determined at all. The condition may occur at any age, more especially between the ages of twenty and forty. Isolated cases have been described at ages varying from nine months to seventy-five years. It is much more common in females, and 75 per cent. of the cases have been postoperative.

1. *Traction of the duodenum* or pressure upon it from various conditions, especially with a low situation of the small intestines in the pelvis and a short mesentery is no doubt a common cause. Here the tightened mesentery may incarcerate the duodenum as it lies on the vertebral column and produce the condition (Kundrat). Albrecht and others, regarded this as a result, and not as the cause of the dilatation. Through dilatation of the stomach the small intestine is held low in the pelvis, and thus pulls upon the mesentery and indirectly compresses the duodenum. This "arteriomesenteric incarceration" thus aggravates the already existing gastrectasis. Whatever be the cause, certainly a large number of cases show at autopsy this constriction of the duodenum, and Bäumler's anatomical proof is worthy of mention. In his classical case there was a very localized constriction near the lower end of the duodenum where it was crossed by the mesentery, and in the mucosa there was a well-defined circular necrosis corresponding to the external compression.

Albrecht demonstrated the fact that at this point the duodenum, even under normal conditions, is more flattened than round, because of the pressure of the overlying mesentery with its superior mesenteric artery, and, as Conner points out, this may be readily demonstrated in the cadaver, as also the increase in the constriction, by gentle downward traction on the mesentery with the finger inserted in the duodenum at this point. The three things considered essential to this are "the dorsal decubitus, an intestine nearly or quite empty of gas and feces, and a mesentery of suitable length — long enough to permit the intestines to slip into the pelvis and yet not so long that they may be supported by the pelvic floor." Perhaps it may be for this reason that lobar pneumonia is sometimes complicated by acute dilatation, owing to the weight of the lungs and violent coughing (Lehmann).

2. *Postoperative or Postnarcotic.* These cases, which are numerous, are remarkable in that few have been recorded in which operation on the stomach itself preceded the dilatation. Abdominal operations of various kinds (gall-bladder, uterus, ovary, kidney, appendix, etc.), as also operations on the extremities for a great variety of conditions have been followed by acute gastric dilatation. In 1918, Collins quoted 188 cases, of which 69 per cent. were postoperative, and 31 non-operative, and due to injury, disease, etc. The interval between anesthesia and the advent of gastric symptoms varied. In most cases the dilatation followed closely upon recovery from the effects of the operation and anesthetic; in others, days or weeks intervened.

The evidence tends to show that in many instances there is a paretic

condition of the gastric muscle, which may be primary or else associated with some toxic condition of unknown origin. Bloodgood has given an analysis of cases observed by him after operation and in association with varying causes, one of the principal being the obstruction which occurs at the junction of the duodenum and jejunum (gastromesenteric ileus). In these cases the enormous distention of the stomach and duodenum is characteristic, and is to be differentiated from high occlusion of the small intestine. Doubtless with acute dilatation there may be additional dilatation of the duodenum with or without constriction at the mesentery, and in other cases, again, much of the small intestine may be concomitantly dilated. The diagnosis of the exact site of the obstruction (if this exist) has an important bearing on the treatment.

3. *Debilitating Conditions.* — (*a*) *General, e. g.*, anemia, rickets, toxic states, certain infections, especially pneumonia, typhoid fever, and miliary tuberculosis, also cardiac disease (Goodhart). These may be the result of various influences which alter the muscular tone of the stomach wall, either indirectly by affecting nervous control, or more directly by toxic action on the muscle. There may be perhaps a neuroparesis though Conner doubts this. In view of the work of Alvarez and Carlson, showing the proliferal automatic mechanism in the gastro-intestinal organ, it is doubtful if the extrinsic nerves have much influence on the genesis of acute dilatation. Gastric tone is the more important factor. The very sudden onset in many patients suggests some special circumstance which the toxic state or nerve lesion has favored; certainly some disturbance, either gastric, nervous, central, peripheral, or reflex, occurs to promote it. The condition is common in children with rachitic manifestations. In 1 case of pneumonia under personal observation the dilatation came on without warning, in a patient who had shown no signs of any gastric distress or abdominal distention half an hour before the extreme dilatation and agonizing symptoms had reached their full development. Lavage gave immediate relief with disappearance of the enormous distention. Six hours later the symptoms recurred quite suddenly with similar results, the patient having rested quietly without distress or distention in the interval. (*b*) *Local:* Previous gastric disease may predispose to the condition, usually through fermentation, giving rise to what has been termed the "gaseous form" of acute dilatation. This is often combined with the etiological types. Excessive secretion has been regarded by some as the primary cause, although there is little to support the view. The fluid has little HCl and usually a great deal of bile, suggesting regurgitation from the duodenum rather than hypersecretion.

4. *Trauma.*—Various forms of trauma are associated with acute dilatation: Head injuries (Erdmann, 1868, Thomson, etc.), with supposed lesions of motor nerves. Spinal injuries, with or without cord symptoms; in one instance (Edmunds) the dilatation appeared five weeks after a paraplegia. Blows on the abdomen (Wallace and Box).

5. *Deformities of the spine* have been frequently observed in patients developing acute dilatation, and in many cases the orthopedic surgeons have been the first to observe the condition. The associated factors are dietetic indiscretions, the restricted cavity of the trunk, and vagal disturbances.

6. *Pressure of a kidney* which had been surgically fixed was the cause in one instance (Oppenheim) and a plaster jacket in another.

7. *Dietetic errors*, combined with great fatigue, may be a factor.

8. *Spasm of the cardia and pylorus combined* was believed by Kelling to initiate the symptoms, and perhaps the association of hypersecretion with acute dilatation.

9. The diseased *pancreas* is regarded by Bardenheuer and Hoffmann as a cause, the former associating the dilatation with trauma, the latter with a chronic inflammation and necrosis.

Pathology.—The stomach is usually of enormous size, often extending down into the pelvis, and may be bent in an irregular U-shape, with the largest half at the fundus. The color is bluish, purple red, or pale; the wall is often thin. Definite pyloric obstruction is rare. The duodenum is dilated partially or throughout in half the cases. Sometimes the dilatation definitely stops near the lower end of the duodenum where the mesentery crosses, and may compress it against the vertebral column. At other times the dilatation extends throughout the whole of the small intestines.

Symptoms.—Mild and severe cases are found, the mild ones being slow of cure, with emaciation, weakness, and prolonged convalescence. The symptoms are usually acute and without previous signs of gastric disease, closely resembling those of intestinal obstruction, for which, indeed, they are frequently mistaken. There is acute abdominal *distress* with *distention*, pain in the epigastric or umbilical region, or perhaps in the left hypochrondrium, with dyspnœa, increase in the pulse and respiration rates, but no fever. *Vomiting*, which is almost invariably present, appears early, as a rule, and is persistent. The vomitus is a dark brown fluid, very abundant, often amounting to many quarts, containing bile and sometimes traces of blood. The odor is usually foul but not fecal. Hydrochloric acid is a very variable quantity and lactic acid is sometimes present. Hydrogen sulphide has been noted in several instances. Lavage, if carried out, empties the stomach of liters of such contents, the removal of which gives immediate relief. Constipation, diminished output of urine, marked thirst, and other signs of dehydration are present.

Objective Signs.—*Inspection* often shows the outlines of a distended stomach, which disappears partially after vomiting, and totally after lavage. There is neither rigidity nor visible peristalsis in the majority of cases. *Palpation* usually shows tenderness and sometimes the firm, tense cushion of the dilated stomach, and but little else, unless increased resistance in the left hypochondrium and a succussion splash. *Percussion* reveals diminution of the tympanitic gastric area and its replacement by dulness, especially on the left side of the abdomen and below the navel, reaching up as high as the right costal margin. This is an important diagnostic sign. Stockton emphasis the occasional coexistence of aërophagia with distention. In fatal cases there is collapse with the hippocratic facies; in case of recovery the stomach returns to its normal size in a few days or weeks.

Diagnosis.—The condition is usually mistaken for some acute abdominal disease, especially perforative peritonitis or intestinal obstruction, and operation is frequently undertaken unnecessarily. The diagnosis

requires a careful anamnesis. Of 60 recorded cases, only 13 were rightly diagnosed. The diagnostic features are the onset, with pain, collapse, and absence of fever, abdominal distention and localized left-sided dulness, with uncontrollable vomiting of large quantities of fluid containing bile, and having no fecal odor. The relief of symptoms and signs after lavage and postural treatment (knee and elbow position) are important confirmatory signs. The differential features of high intestinal occlusion are mentioned by Bloodgood as follows: "Initial pain, accompanied perhaps by peritoneal shock, which may later somewhat disappear, and vomiting without marked distention." In acute dilatation the initial pain is often absent, there is epigastric distress and gradual and progressive collapse. Epigastric distress is early and relieved by lavage in acute dilatation, but is much later in high intestinal obstruction. Among other conditions with which it may be confused are post-anesthetic vomiting, acute pancreatitis, and uremia.

Prognosis.—The outlook is bad if the diagnosis be not made early and suitable treatment adopted; 47 out of 64 cases published died. In Conner's series of 102 cases, 74 died, although, as he remarks, many unreported cases recover where either the condition was mild or unrecognized. In 75 per cent. of Conner's cases the duration was less than five days, and in a few instances the patients died within three hours from the onset of the symptoms. If the complication does not end fatally, some impairment of motor power usually persists. The symptoms may disappear at once after treatment, or days and weeks may elapse before complete recovery.

Treatment. Early recognition is essential and early lavage is important with the head low and the pelvis high; one is otherwise very apt not to reach the fluid at all. It is of great importance to thoroughly wash out the organ, at first often, later on less frequently. No food should be given by the mouth until recovery has sufficiently advanced, and one should use water enemata or subcutaneous saline infusions instead. Stimulants should be given as required. *Operation* is of no benefit unless after lavage there is no improvement, in which case some severe intestinal obstruction may be suspected. In these cases the probable incarceration of the duodenum requires special treatment. Schnitzler first pointed out the benefits to be gained by turning the patients over from the dorsal position, and the knee and elbow posture has been successful.

When such measures fail, operation may be tried, although hitherto the results of gastro-enterostomy have been far from encouraging. Bloodgood's study of the condition has led him to believe that it is well to regard these cases as probably instances of gastroduodenal dilatation, and if lavage fails the duodenum should be carefully explored. If the dilatation be purely gastric, then gastrostomy or gastrojejunostomy should be performed, whereas if the duodenum too is involved, jejunostomy or duodenojejunostomy is preferable. Borchardt, quoted by Conner, states that when other methods of treatment have failed, it is doubtful if operation will meet with any greater success.

Chronic Dilatation.—Varieties.—There are two forms: (1) Idiopathic, or absolute, otherwise called primary or atonic; simple gastrectasis; myasthenia gastrica; and (2) symptomatic, or relative, otherwise called

secondary or obstructive—the result of stenosis of the pylorus—usually hypertonic and mechanical. There is either benign or malignant obstruction and rarely the duodenum is the seat of the stenosis. Allbutt suggests the term extension as including especially the cases of idiopathic dilatation. The diagnosis of *idiopathic dilatation* can only be made by prolonged observation to exclude stenosis. Gastric analysis shows retention of food, with all the evidence of gastrectasis. Surgeons, too, find this condition not uncommon, and operate for gastrectasis when careful search fails to reveal any signs of obstruction at the pylorus. Mikulicz thought them not infrequent.

The walls lose their resiliency and the viscus expands, becoming gradually less able to handle the ingested food, especially when in large quantities and stagnation follows.

Etiology.—Though commonest in middle-aged adults, it occurs sometimes among rachitic children (Ladd). Two classes of causes exist, local and general. *Local conditions* are trauma, improper clothing, laparotomy, repeated pregnancies, chronic gastric disease of any kind, especially if with fermentation (Cohnheim's so-called vinegar and gas factory) and excessive improper food, whether in quantity or quality.

Kaufmann describes two classes of patients: (1) In the one there is variable secretion (high or low), with atony; the symptoms are really due to the atony, and are cured by lessening it. (2) In the second there is variable secretion without atony. Such cases come under the category of neuroses, *e. g.*, hyperesthesia of the gastric mucous membrane, and resemble similar conditions in other organs (*e. g.*, cardiac neuroses, nervous diarrhœa, etc.); *i. e.*, gastric neuroses so-called. Such patients need no local therapy for the stomach but rather general treatment.

Gastroptosis frequently accompanies gastrectasis. A progressive stenosis with increasing motor insufficiency may occur from kinking at the pylorus. Steele and Francine found in 70 patients with gastroptosis that dilatation existed in all. The degree, however, must be very slight for gastroptosis without indigestion is extremely common.

General Causes.—The habitus or type, heredity, and any general weakness from whatever cause, may induce some motor weakness of the viscus. Fevers, toxic conditions and nervous states all favor it, as do all forms of anemia.

Relative, Symptomatic, or Obstructive Gastrectasis (From Stenosis).—The causes of stenosis are numerous; *spasm* with gastric ulcer, erosions and scars (never from neuroses) (Cohnheim); *foreign bodies: e. g.*, resin balls from swallowing shellac spirit for ten years, hair balls, cherry stones (Crämer), gall stones and beans and peas (Fleiner), (such bodies may remain for three months); *hypertrophic pyloric stenosis;* polypi; tumors (Crämer); scarred ulcers; *cancer* of the pylorus and of the lesser curvature extending to the pylorus. *Tumors outside the stomach* (*e. g.*, of the liver or gall-bladder, pancreatic tumors pressing on the duodenum, floating spleen with pressure on the duodenum, movable kidney, dermoids, enlarged glands, etc.) may be a cause. *Perigastritis:* inflammation outside of the stomach and associated with neighboring organs, *e. g.*, liver, gall-bladder, pancreas; cicatricial puckering associated with cholelithiasis, perigastritis, etc.; epigastric hernia; appendicitis with or

without adhesions; omental adhesions from appendicitis, especially if to the linea alba; torsion, flexure, and kinking of the duodenum at the duodenojejunal fold in enteroptosis; trauma, producing inflammations near the pylorus, hematoma of the wall, or spasm of the pylorus.

Pathology.—The dilatation varies in degree and character. The one anatomical feature is the altered size of the organ, although that is not always increased even with marked motor insufficiency; sometimes it is monstrous and may seem to fill the entire abdominal cavity. In Strauss' case of stenosis from an old ulcer the stomach held five and a half liters. Much larger dilatations are mentioned. Jadow's case in which the capacity was 45 liters is worthy of mention, if true.

The gastrectasis may be partial and is sometimes diverticular. Dilatation begins in the lowest portions and those most overtasked, the fundus, pylorus, and greater curvature. Later it becomes general. The other abdominal viscera are in extreme cases compressed and pushed in various directions. The spleen and liver may lie abnormally high while the small intestines are pushed downward. The thickness of the stomach wall varies. In one case with chronic inflammation (Lebert) it was 14 mm. thick. It is especially in the obstructive cases that this increase occurs, although even in idiopathic cases it may be abnormally thick. As a rule, when no stenosis exists the gastric wall is thin and atrophic. The *mucous membrane* may be thickened, hypertrophic, or irregular and hard, a condition usually existing when chronic gastritis is also present. Sometimes the mucosa is thinned and atrophic, and not at all infrequently atrophy and hypertrophy alternate in the same mucous membrane. The muscle is changed, its appearance depending on the cause and pathological condition. With pyloric stenosis, especially if benign, there is muscular hypertrophy (compensatory), while in idiopathic cases the atrophied muscle is but a feature of the general myasthenia. Fatty and colloid changes are often seen in microscopic preparations. The interstitial tissue is often infiltrated in the chronic cases with increased fibrous tissue and small round cells, while in the acute cases there may be small round cells, extravasated blood cells, and separation of muscle and fibrous tissue cells.

Symptoms.—These vary according to the degree. In mild cases there may be but a few digestive disturbances, mental torpor, thirst, anorexia, constipation, and diminished urine, with little evidence of any serious condition. This, too, occurs in the early stages of the more serious types. Advanced cases from whatever cause show certain general symptoms in common, a dry skin and cold extremities.

Dyspeptic symptoms develop early. The appetite is usually diminished (unless hyperacidity exists from some benign stenosis), the breath is sour, and flatulence and pyrosis are present. Thirst is often a distressing symptom, and corresponds to the amount of retention and the degree of motor insufficiency, of which it is therefore a good criterion. *Constipation* is marked and there is atony of the bowel. Dry, hard scybala are often passed with colicky pains; piles and fissures form. The degree of constipation is a good criterion as to the degree of motor insufficiency. *Diarrhœa* is rare but sometimes alternates with constipation; mucous colitis may coexist. *Emaciation* occurs in proportion to the degree of dilatation, and is worse if the intestines are deranged.

Pain is less marked in idiopathic than in obstructive cases. In obstructive cases, especially if from ulcer or spasm, or cancer, it is often intense. *Vomiting* is not so constant in idiopathic as in obstructive cases. In the latter it is as a rule periodical and explosive after every few meals. The amount has no relation to the previous meal, and the vomitus consists of food from days or weeks before. It is thus copious, and may amount to several quarts. Later there may be little or no vomiting because the walls are weakened and the condition then becomes serious. The contents are usually of a dark gray brown. There are three layers, froth on top, fluid in the middle, while the sediment below contains yeast, sarcinæ, mucus, and food (new and old). Mucus, if abundant, suggests a concomitant gastritis. Microscopically, one sees bacteria, fatty acid crystals, epithelial cells, sometimes blood cells and pigment. There is an odor of fermentation and organic acids may be abundant. The finding of lactic acid is important only when in the fasting contents or after a test meal. HCl may be in excess, deficient, or normal.

The Urine.—Corresponding to the amount of retention, so is the diminution in the renal secretion. It forms a good basis for measurement of the gastrectasis and is also a guide to prognosis and treatment. Increase in the urine indicates improvement. The specific gravity is high. The chlorides are lessened and the phosphates increased. If much hyperacidity is present the urine may be alkaline. Albumin, acetone and diacetic acid are sometimes present.

Cardiovascular symptoms are common: Palpitation, anginoid attacks, dyspnœa, and throbbing sensations. The pulse is often weak and irregular and the blood shows secondary anemia.

The *temperature* is lowered and the patients feel chilly from slight causes. More rarely there are febrile attacks from a concomitant gastritis or toxic causes.

The nervous symptoms are varied. Languor, apathy, depression of spirits, and melancholia are common features. Headache and dizziness are frequent. Mild psychoses, insomnia, deafness, etc., are common manifestations, and when coming on at a regular time are regarded by patients as the cause rather than the effect of the malady. These are probably the result of dryness of the tissues, inanition, and toxemia.

Tetany is worthy of special notice. Mentioned by Morgagni, it was first described by Newman in 1861, and later by Steinheim, while Kussmaul gave it prominence as a classical feature of dilatation in 1869. This condition, although common to various diseases of the gastro-intestinal tract, is chiefly associated with pyloric obstruction in which dilatation, hypertrophy of the stomach wall, with hyperacidity and hypersecretion are present. It occurs more commonly with benign stenosis, and is rare in obstruction from malignant disease or from external pressure. The attacks appear after severe and persistent vomiting, and after lavage. The stomach should be emptied some hours before lavage is practised to avoid the onset and recurrence of the attacks. The duration may be from a few minutes, to hours, days, or weeks. When prolonged it ends usually fatally. Mild grades are common and probably often overlooked. Muscular twitchings, prickling sensations, etc., in gastrectasis are doubtless warnings to urge surgical intervention. Crämer's view was that

any gastrectasis not vastly improved in four weeks under lavage, dieting, and massage should be subjected to operation.

Various theories exist as to the causation of tetany. That most recently accepted follows the work of W. G. MacCallum and others, viz: that the calcium content of the blood is reduced, while the carbonates are increased. It may occur even if the parathyroids are healthy.

The prognosis in tetany is always grave, and the average mortality has been given as 70 to 80 per cent. There were 31 deaths in 40 cases (Albu). Death usually follows only after the tetany has been well developed, from failure in treatment. Patients who pass successfully some attacks of tetany, are liable to recurrence of attacks.

Treatment of Tetany.—Medical treatment may be tried for a short time, but surgical interference should not be delayed too long when lavage and medicines fail. Calcium chloride (10 cc. of a 10 per cent. solution intravenously) is often useful. The one efficacious method, where stenosis exists, is the surgical one which provides proper drainage by a gastro-enterostomy.

Physical Signs of Gastrectasis.—*Without stenosis*, there may be no evidence on inspection, or the bulging stomach may be visible in outline and on palpitation the air cushion may be felt. Usually the stomach is lower than normal. The roentgen-ray reveals delay without much increase in motor function. The chemical analysis varies with the cause; the secretion may be diminished or excessive. There is nothing characteristic.

With Pyloric Stenosis.—Gastrectasis, under these conditions, offers a much more definite picture. The stomach outline is clearly visible, as a rule, and is usually somewhat larger and lower than normal. Peristaltic and antiperistaltic waves are seen, or may be induced by flicking the abdomen. Very often the tumor, if present, may be seen. Palpation reveals the rigidity characteristic of motor spasm under this condition (Magensteifung). Percussion usually enables one to outline the enlarged organ. The chemical analysis varies according to the etiological factor. The fasting contents are always abundant, while the roentgen-ray shows the stenosis, the increased peristalsis, and stagnation or retention of food. Examination after the administration of bismuth may enable one to see the outlines and the less active fundus; one may also see the pylorus open intermittently and the impaction of masses in imperfect solution prolonging the closure of the pylorus.

Diagnosis.—The various considerations may be tabulated thus: (1) As to the presence of gastrectasis. (2) If present, as to its nature, *i. e.*, idiopathic or obstructive. (3) If obstructive, as to the nature, *i. e.*, benign or malignant stenosis. (4) If probably benign, as to its special form, viz., spasm, foreign body, hypertrophic stenosis, intragastric tumor, extragastric tumor, inflammation, etc.

Gastrectasis must be distinguished from several conditions. *From dilated colon:* One must make repeated examinations at various hours and empty the stomach by siphonage. It is often hard to tell without such tests, and it may be well to inflate the colon from the rectum. The history and symptoms will assist in the decision. Absence of splenic dulness in itself is of little importance in the diagnosis, being merely an

aid. One must exclude emphysema, pneumothorax, and diaphragmatic hernia. Moreover, one must look for a cause, movable or diseased kidney, umbilical hernia, tumor, etc. If necessary, an anesthetic should be used. *From Gastroptosis:* In simple dilatation, the lesser curvature is in its normal position, while if there be gastroptosis, the site will be lower than normal, and the position of the stomach may be vertical, horizontal, or otherwise. In simple gastroptosis there is no sign of motor insufficiency after a test meal. The fluoroscope and skiagraphic picture aid the diagnosis. *From Nervous Dyspepsia (without Motor Insufficiency):* The symptoms are out of all proportion to the organic changes, and there are various stigmata of a neurosis. *From Chronic Gastritis:* The stomach is of normal size and the motor power normal or nearly so (unless dilatation coexists, as it usually does later on). There is a history of the cause, and much mucus is vomited. *From Hypersecretion:* After complete lavage of the stomach on the previous evening there is abundant gastric juice found in the early morning (more than 40 cc. should be present to make a diagnosis of hypersecretion). *From Gastric Crises:* These present one feature resembling gastrectasis, viz., the marked and copious vomiting, not, however, of retained food, but of concentrated gastric juice and mucus. Gastric digestion is usually normal in the intervals between the attacks. Other conditions, *e. g.*, ovarian tumors, dilated gall-bladder, sacculated peritoneal exudates, and pancreatic cysts should offer no difficulty. Sometimes a *spindle-shaped dilatation of the œsophagus* may occasion doubt because of the periodical vomiting of food from previous days. This may be hard to differentiate. The stomach, however, is not enlarged, the introduced tube causes immediate vomiting of alkaline material, while if the tube be pushed farther it reaches the stomach and withdraws acid contents.

Varieties of Pyloric Stenosis.—*Pylorospasm.*—This occurs at the height of digestion, as a rule, and may be constant or periodical, resulting in temporary closure of the pylorus with retention of food. There may be severe pains, vomiting, and signs of motor insufficiency, such as thirst, diminished urine, constipation, and enlarged gastric area. The vomitus is hyperacid, and there is often hypersecretion. The vomiting relieves the discomfort until the cycle recurs. Analysis shows stasis, increase of HCl, sarcinæ, yeast, fatty acid crystals, and signs of marked fermentation. The pyloric area is tender and may show tonic contractions, while palpation of the fundus may reveal the characteristic rigidity (*Magensteifung*). The prognosis is more favorable, although recurrences are frequent.

Cicatricial stenosis of the pylorus (the type is the scarred ulcer, although caustics, etc., may induce it). The history is of importance, especially the record of previous hematemesis or of recurrent attacks of vomiting and pain ("indigestion"). The signs of progressive stenosis, as seen on physical examination, gastric analysis, and examination of the stools for occult bleedings, are likewise important.

Duodenal stenosis may be indistinguishable, unless the obstruction be infra-ampullary, in which case there will be a constant back flow of bile into the stomach. Stenosis of the duodenum usually occurs from cancer,

pressure of benign tumors, scarred ulcer, localized peritonitis, gall-stones, malformations, etc.

Perigastric adhesions with pyloric stenosis (cholelithiasis, inflammation, etc.). Here, too, the history is of great importance, also the physical signs, the presence of jaundice previously, and bile in the urine.

Stenosis from external pressure occurs from enlarged glands, dermoids, new-growths, and inflammatory exudates, also from kinking or constriction through fibrous bands, etc., as also from traction as occurs in acute dilatation where the duodenum is constricted through traction of an arteriomesenteric fold.

Impaction of food or foreign bodies in the pylorus may be the cause or *benign tumors* within the pylorus, *e. g.*, polypi.

Hypertrophic stenosis, the so-called stenosing gastritis. The condition is probably a rare one, arising from different causes and presenting as its two main features at first a chronic gastritis and later the signs of motor insufficiency with stenosis. There are no cicatrices and no tumors, but a diffuse thickening of muscle or fibrous tissue may be present, a localized benign stenosis. Quite a number of isolated cases are on record (Boas, Habershon, Tassia, Tilger, etc.). The condition has been found most commonly in middle age, runs a slow course over years, with exacerbations and remission of symptoms (chiefly those of gastritis followed by stenosis). There is anorexia and emaciation. The gastric analyses vary. It is not easy to distinguish from a scarred ulcer which may have been latent for years, but the diagnostic features are those found in the general picture with its protracted duration. In descriptions given by Russell and by Maylard, cases of adult stenosis of congenital origin are described with symptoms of varying intensity, and these writers conclude, whether or not on sufficient proof, that such cases are very common indeed. It seems, however, not always easy to prove the existence of a stenosis during operation, and the mere improvement after gastro-enterostomy should not of itself convince one that a pyloric stenosis had been present—still less that it was congenital.

Stenosis from Malignant Disease of the Stomach.—The following table outlines the differences from benign conditions causing stenosis:

	Benign.	Malignant.
History.	Ulcer, toxic gastritis, caustics, etc.	Previous normal digestion, perhaps.
Age.	Any age.	Usually after forty years of age; not infrequently earlier, however.
Course.	Rapid, but with less marked decline in health.	Rapid and progressive development of weakness, etc.
Tumor.	Smooth, often more movable.	Nodular, hard, fixed.
Secretions and contents.	HCl normal or excessive; no lactic or butyric acid; H_2S present sometimes; few or no Boas-Oppler bacilli; sarcinæ long present.	HCl less or absent; lactic and butyric acids often present; H_2S uncommon; Boas-Oppler bacilli common; sarcinæ uncommon, and soon disappear.
Roentgen-ray.	No filling defect. Hyperperistalsis.	Filling defect. Fixation of wall and local hypoperistalsis.
Therapeutic	Sometimes nutrient enemata benefit.	Nutrient enemata useless.
Metastases.	None.	Usually sooner or later.

Course of Gastrectasis.—The cause determines not only the duration but also the essential features and symptoms. Idiopathic cases are slow in development, and their course depends on the persistence of the exciting cause and the possibility of its removal. Patients who have long been the victims of the disease in an advanced stage will be difficult to relieve. With early and suitable treatment the condition is often held in check and development will extend over years. Thus the idiopathic cases and those due to pylorospasm, being more amenable to therapy, will run a mild course and last a shorter time than those associated with stenosis. Pyloric obstruction causes a more or less rapid development of symptoms, rapid when the obstruction develops quickly, as in carcinoma, subacute perigastritis, etc., more slowly with gradual cicatrization of an ulcer at the pylorus. When benign stenosis exists, its special nature, its degree, extent, and curability, the condition of the muscular wall of the stomach, and the early diagnosis determine the probable duration. If not relieved by appropriate treatment these patients get rapidly worse and fail from inanition; surgical intervention (gastroenterostomy) may alter the whole course of the malady, and quickly bring about recovery even after advanced disease exists.

The stenosis of luetic origin may improve under specific treatment, or else the newly formed scars which result from the effect of specific treatment upon the healing process may also increase the stenosis. Cancerous stenoses, of course, run a progressively downward and usually a rapid course unless removal of the neoplasm is carried out. Under rare conditions, they improve markedly for a time, either because the pylorus is reopened through breaking down of the obstructing cancerous mass, or because of the effects of general treatment.

The occurrence of gastritis and intestinal disease lengthens the duration of the malady and adds to the difficulties of cure. Relapses are very common in the idiopathic cases, and are usually dependent on indiscretions of diet or excesses. Persistence in the exacting treatment is by no means easy, and the tendency to relax in care makes it difficult for patients to lead the model life required for permanent cure.

Prognosis.—In the early stages of gastrectasis one should carefully guard against a too definite assurance as to the cause and probable outcome. The two features which govern the prognosis are the cause and the possibility of its removal. Cures are possible in idiopathic cases that are even advanced, provided the wall of the stomach is not permanently damaged and the general condition of the patient capable of improvement. Gastroptosis renders these cases much more difficult of cure. Early cases are of course always amenable to cure if the proper treatment be employed and conscientiously carried out. The normal amount of urine, the lessened degree of thirst, the good condition of the musculature, and possibility of obtaining suitable diet are all favorable features. The onset of tetany is a serious complication and one of grave omen. Relapses are common and due recognition of their frequency is important in dealing with prognosis. In obstructive cases the cure is always possible, except in malignant disease, for surgical intervention, with a new opening to short-circuit the passage, renders a benign stenosis of no importance in itself.

Prophylaxis.—Proper hygiene, diet, and mode of life are essential to the prevention of pure gastrectasis from atony of the stomach, as is also moderation in the use of food and drink. Special care in debilitated states, as to diet, exercise, and habits, must be carefully remembered, and one should avoid the causes of idiopathic dilatation.

Treatment.—A detailed diagnosis as to the nature of the gastrectasis is essential to rational *treatment*, which should be based on (*a*) the etiology as regards food, drink, and habits, and (*b*) the social state, history, family history, previous diseases, and conditions of the viscera. In all patients with motor insufficiency certain general rules apply, no matter what the cause or underlying condition may be. The stomach must be as far as possible emptied within the normal time, and stagnation and retention of food avoided. Food must be administered of a kind which, as regards quantity and quality, will not excessively burden the stomach. The motor power being weak, one must aid its activity by avoiding unnecessary effort on the part of the gastric muscle, while fermentation must be avoided or reduced to a minimum. Where pyloric stenosis exists surgical intervention must be carefully considered. In the benign cases it is often curative.

Diet.—The main objects are as follows: (*a*) To supply sufficient nutriment in an easily assimilable form, (*b*) to avoid over-burdening the weakened stomach with bulky foods, (*c*) to avoid fermentation and retention of foods, (*d*) to give foods of such kinds and in such a way as to assist their early propulsion into the intestines where the chief digestive function is carried on, and (*e*) to supply enough fluid to the body to fulfil the requirements of tissue thirst. These results are best obtained by giving frequent small meals, six small meals daily rather than three of ordinary amount. Food must be given either in soupy form, or as dry, solid food in a finely divided form. It must be taken slowly and well masticated; for this reason the teeth must be kept in good condition. The patients must rest before and after food, preferably in a recumbent position, on the right side. Occasionally lavage assists materially. This principle depends on the evidence given some years ago by von Mering, that water is not absorbed in the stomach, so that its propulsion into the intestine is necessary for its usefulness to the tissues.

In any case much fluid should be avoided; milk with cereals, *e. g.*, barley, rice, oatmeal, etc., or one of the numerous concentrated albuminous foods may be given. One may add cream or make a custard. Bouillon with eggs makes an excellent form of concentrated nourishment, and is usually readily assimilated; so also are meat juices and meat jellies. The dry foods and those more solid should be prepared in a finely divided form, especially the meats and vegetables.

Whatever meats are used should be chopped up and well masticated. Scraped raw beef, tender roast beef or fillet, thinly sliced smoked ham, oysters, and sweetbreads are often well borne, as also chicken, pigeon, tender mutton, and white fish of various kinds. Vegetables must be mashed or in purée form. Only the less coarse varieties and those with least cellulose should be employed. Purées of potatoes, peas, spinach, asparagus-tops, or cauliflower can usually be taken with ease. Bread

may be given, preferably white stale bread, or toasted, or one may use rusks and unsweetened biscuits. Fats, notably milk fat, are good, especially with the addition of HCl. Alcohol is of value only when weakness is great. It should be remembered that alcohol induces an increased secretion of water into the stomach. Malt extract in small amounts may aid the appetite.

To some extent the diet must depend on the results of gastric analysis. With *subacidity,* cereals are preferred rather than albumins, and whatever meats are used should be finely divided before eating. White meats are preferable, and dry white fish is usually well borne. Vegetables, even though better taken than proteins, must be finely divided and given in limited amount. In these cases the use of drinking water to which a little diluted HCl has been added is often beneficial; it should be sipped slowly after food. With hypersecretion one should select mainly albuminous foods, meat, milk, eggs, and fats in moderate amount, of which butter is the most easily borne. Starches should be carefully restricted, although rusks and dry toast are suitable. Sweets should either be much limited or altogether avoided. Fluids are more tolerated than in subacidity, especially the still alkaline waters. *Saline enemata* are often most useful to relieve thirst in idiopathic dilatation.

Of *mechanical measures* the most important is thorough lavage of the stomach. As a rule, early mild cases merely require strict attention to diet and daily regimen to effect a cure. One must judge according to the individual case how much lavage is necessary. In the moderately severe cases the stomach is never empty during the course of the day, food being retained until the subsequent meal, but the stomach empties itself during the night. In such cases a careful lavage given before the evening meal does good by removing the fermenting products of the day's feeding, and a small appropriate meal taken thereafter on an empty and cleaned stomach is commendable.

In the very severe cases when food remains in the stomach overnight, and has not been propelled into the intestine by early morning, thorough lavage is still more imperative, sometimes twice daily. Lukewarm water suffices for the purpose, although when much fermentation is present, salicylic acid solution (1 to 1000) may be used. How long should one keep up lavage? This must depend on the persistence of motor insufficiency. It should be done daily until we are sure the digestion is not delayed overnight. The lavage should be discontinued gradually.

Other mechanical measures are of less importance, although often of benefit. Massage is beneficial in a general way, but should be used systematically, and under proper skilled direction. It assists in obviating the chronic and often most persistent constipation. It should not be done until at least one and a half hours after any meal.

Hydrotherapy is of the greatest benefit; in fact, apart from lavage, there is no mechanical treatment so beneficial in gastrectasis. When hydropathic apparatus is not available, much benefit is gained from daily cold baths, followed by dry friction with a rough towel. The use of compresses over the stomach at night covered with oiled silk and a binder often gives great relief.

Bandages of a supporting nature, or proper-fitting corsets for women which support from the pelvis, are useful; such corsets are constricted about the hips, but are loose about the epigastrium and lower part of the thorax, thus affording room for breathing, and not allowing the stomach to be without support from below. These are especially useful when gastroptosis exists. Bulky harness should be avoided.

Electricity has merely a general value and its direct local action is very dubious. Experiments on dogs have shown that faradism does not directly affect the gastric muscle, but causes contraction merely of the external abdominal muscles. Apart from this general effect, electricity is but another form of suggestive therapeutics.

Drugs form the least satisfactory of all methods in the treatment of gastrectasis. No drug that is known can effectually contract the dilated organ or act with continuous benefit upon the gastric muscle. Strychnine is much used for this purpose, although but little evidence exists to prove that its value is other than as a general tonic. The drug therapy is purely a symptomatic one. When hypersecretion exists, relief is often obtained from atropine in small doses (gr. $\frac{1}{100}$) at night, or if need be in the morning as well. Alkalis have perhaps an indirect value in neutralizing an excess of acid, although they have no effect in diminishing the secretion. For subacidity the use of well-diluted HCl sipped in a tumbler slowly every few minutes after food seems to aid digestion, or at all events to give comfort. In moderately severe cases the writer has had beneficial results from the use of olive oil, in dessertspoonful doses after food, as recommended by Cohnheim who preferred its administration through the tube in doses of 200 to 500 cc.

Constipation requires varying treatment according to its degree of severity. In mild cases no drugs are required, and proper feeding, massage, exercise and perhaps occasional water enemata will suffice. It is often useful to administer Rochelle or Sprudel salts in small doses in the early morning, after which the patient takes moderate exercise for a short time previous to breakfast. In any case drastic purgatives do harm, and only mildly acting drugs are to be recommended. Should these fail in the more severe forms of dilatation, reliance must be placed on enemata every other day. Daily evacuations are not necessary to health, and patients should be advised accordingly.

Vomiting should be controlled by proper diet and by lavage. When these are ineffectual and in persistent cases surgical intervention is necessary. For the thirst the proper use of saline rectal injections will aid, and the mouth should be frequently rinsed with some pleasant wash.

Surgical.—The indications for operative interference include three types of cases: (1) Acute cases when medical treatment has failed or is known to be useless, *e. g.*, with twisting of the duodenum. (2) Pyloric stenosis, whether for removal of adhesions, fibrous bands, tumors obstructing the orifice, external compression from any cause, or when relief is impossible unless one is enabled to create a new passage for the food. (3) Idiopathic dilatation without marked gastroptosis or general enteroptosis, when medical treatment has been unsuccessfully tried, and when, in consequence, the patient is losing in weight and strength

from insufficient nutriment, or again, when the symptoms even though not grave, are sufficiently irksome to interfere with daily routine.

Two objects are to be attained: (1) To remove the cause; (2) to remove the results. The methods are: (1) Resection of the pylorus, pylorectomy. (2) Pyloroplasty. (3) Gastro-enterostomy. (4) Bircher's gastroplication, which reefs up the anterior wall diminishes the size of the stomach. This latter was advocated by Keen, Weir, and Brandt. Eight of Bircher's 10 cases did well. Gastro-enterostomy in uncomplicated cases has given excellent results. Enteroptosis is distinctly a contra-indication to surgical interference—and even mere gastroptosis, if at all marked, is not likely to permit of successful operation in gastrectasis, even although the gastrohepatic omentum be shortened.

"CONGENITAL" HYPERTROPHIC STENOSIS OF THE PYLORUS

Synonyms.—Congenital pylorospasm; hyperemesis lactentium (M. Schmidt); infantile hypertrophic stenosis of pylorus; pyloric disease (Genevrier). The first accurate description is attributed to Beardsley, 1788, though not until one hundred years later was the attention of the profession generally drawn to the disease (Hirschprung).

Pathology.—Two distinct conditions seem to exist:

1. **Pylorospasm.**—This, without true hypertrophy, is described by Pfaundler in systolic and semisystolic stomachs, a pseudohypertrophy. The condition is often seen at operation and autopsy, for fixation of the muscle occurs during certain phases of digestion. Heubner and Freund share this view. Holt, Ramsay, and others are dubious as to the existence of this condition. Holt believed that spasm is merely a symptom added to those already existing as a cause of hypertrophy. These cases must be regarded in the light of mild types, of short, perhaps, intermittent course, and not requiring surgical intervention because there is no permanent anatomical disturbance.

2. **True Hypertrophy.**—The pyloric ring is increased in size and thickness, owing to hypertrophy of the muscular fibres, chiefly the circular ones, although it is difficult to measure to what degree the longitudinal muscle shares in the increase. The swelling is sharply delineated at its duodenal end, but shades gradually into the musculature of the pyloric canal. The mucous membrane is folded up and the submucosa is little, if at all, altered. The lumen is small. The stomach is dilated, and in cases of long standing often shows a diffuse hyperplasia of its muscle. The duodenum is empty. It is quite conceivable that all transitions may occur between mere spasm and true hypertrophy. Most authorities to-day recognize mild and severe types.

Pathogenesis.—The condition is much more common in males, in the proportion of 10 to 1 female, more frequent in the firstborn, and in infants who are artificially fed. The exact etiology is still undetermined, and if primarily a congenital hypertrophy of the circular muscles of the pylorus or a local pyloric spasm from pre-existing ulcer, fissure or erosion, with secondary hypertrophy, remains still in doubt. The work of Cunningham, Stiles, and others has thrown much light on the anatomical condition.

Normally, the stomach may be considered as an organ in which the pylorus is a distinct and separate portion, with a function both to expel and to retain food. The cylindrical canal, which is about 2 to 3 cm. long, is contracted at birth, and its lumen is obliterated by the folds of mucous membrane. The ring projects normally into the duodenum in a way similar to that in which the cervix protrudes into the vagina. The muscular fibres of the pylorus are so arranged that the circular ones, which surround the whole length of the canal, are to some degree antagonized by the longitudinal bundles, which as Cunningham shows are derived from the body of the stomach, and spread about, in gradually increasing numbers over the pylorus, and dipping even into the submucosa, aiding in relaxa-

FIG. 41

Congenital stenosis of the pylorus. *A*, pylorus; *B*, hypertrophied muscularis.

tion of the sphincter. Between the circular fibres of the pylorus and those of the duodenum there is a dividing band of connective tissue. In the cadaver the pyloric canal is usually tightly closed, so also probably during life except during digestion, when it opens irregularly and intermittently. When pyloric stenosis exists, the whole canal is probably involved, and the changes are primary, while any lesions in the stomach elsewhere are secondary.

Other conditions of a mild nature, such as recover readily on medical treatment, may be regarded as due, in most instances, to obstruction of the pyloric lumen from swollen membrane or an inspissated mucous plug, a condition, too, that one might readily conceive to be associated

with spasm. Such a case was described by Scholten, in which a true thickened membrane was observed at operation and at postmortem.

Doubtless the earlier observers had the correct view in regarding the condition as developmental hyperplasia of the pyloric muscle, a congenital redundancy, or prenatal overgrowth (Nicholl, Cautley, Ibrahim). The fact that the pylorus first appears in fetal life at the third month shows that enough time exists before birth for excessive growth, while the degree often found excludes the possibility of postnatal development. Ramsay and Downes are of the opinion that at first congenital hypertrophy exists with gastric stagnation, that the increased muscular action causes a circulatory change, with resulting œdema, and this completes the obstruction. Dent describes a case in a fetus of seven months. In the newborn, the pylorus is relatively thick, and later becomes thinner: if the thickness persists, or if there are digestive disturbances, the mucous membrane becomes thickened, and a pathological condition occurs with symptoms. Sometimes when pyloric stenosis occurs as a congenital condition, other parts of the body show abnormalities, *e. g.*, there may be congenital atresia of the anus; in Thomson's series of 100 cases, 11 showed hereditary tendencies in females, while in only 2 were other congenital lesions present. Torkel, in 1905, cites an instance in which, on anatomical grounds, a proof exists of a congenital origin, aberrant embryonic tissue (Brunner's glands) being found amid the fully developed structures.

The *neoplastic* theory ascribes to it the nature of a benign adenomyoma, and some of the cases seem to justify this conclusion. The name "choristoma" has been used.

A *nervous* theory was advanced by Thomson and Still, according to which the condition is associated with disturbed coördination of the relaxing and contracting fibres of the pylorus, with increased irritability, and this latter whether originating during intra-uterine or extra-uterine life leads to spasm, and this spasm leads to hypertrophy – a hypertrophy from overwork. However, no proof exists of incoördination or of nervous derangement in fetal life. Nor are we sure that spasm causes the hypertrophy of the pylorus. If this were the case, the same spasms might be expected then from other conditions of irritability, *e. g.*, hyperacidity and faulty feeding, but such have not been shown to occur. Freund, however, regarded hyperchlorhydria as an important factor. Pirie again attributes it all to hyperadrenalism, which by creating first pancreatic insufficiency, accentuates pyloric closure.

Symptoms. The condition is more frequent than was supposed until recently. The infant, frequently the firstborn and more often of the male sex, is healthy at birth; symptoms usually begin to show from the eighth day to eighth week, and very rarely as late as the fourth month. Very few cases are on record in which the symptoms began immediately after birth – a point of great importance in the diagnosis. Cases may go on to adult life and Bassler described authentic instances. Digestive troubles of an intermittent type, especially vomiting, usher in the symptoms. The breast or the bottle is taken reluctantly no matter how careful the feeding, and the child is easily satisfied. When vomiting begins early,

however, the appetite is often maintained in a striking way. *Vomiting* is the chief early sign, is explosive, and often copious according to the degree of retention; it usually represents the entire feeding. At first it seems unimportant, although no adequate cause is found; then its persistence rather than its frequency attracts the attention. Gastric analysis gives variable results.

Signs.—Constipation is the rule, requiring the use of enemata, or more rarely diarrhœa occurs with green, watery stools, containing mucus, and perhaps tarry from the presence of blood. The urine is diminished. Wasting is sometimes rapid, and there may be marked weakness, the result of the starvation, the condition resembling and often being mistaken for marasmus. The child is often in severe pain, with violent cramps and epigastric resistance, and cries out or whines; at other times it is quiet and dull. Thomson considers the absence of crying a feature in the diagnosis.

Dilatation.—Sometimes the stomach region bulges if the organ be full, and the dilated viscus may be seen extending to the navel. Dilatation is often marked; in one of Henschell's cases the stomach held 400 cc. Heubner found the majority of cases with undistended stomach, which he attributed to the constant vomiting. Dilatation is perhaps more common with bottle-fed infants. *Visible peristalsis* is most marked in long-standing cases, although Sarvonat and Audry described it in a child aged two weeks. Probably when mere pyloric spasm exists, without true hypertrophy, there is much less peristalsis. It is an important sign when present, although not always found, and often only at long intervals especially after food. The *tumor* may be palpable, is sometimes lower than, and sometimes beneath the enlarged liver, as a hard cylindrical or spherical lump, the size of a filbert, which may even be felt to contract and to change in hardness during peristalsis. The fluorescent screen often reveals a typical picture, that of a large cavity with increased peristalsis, the waves being marked in the upper pole of the stomach, while the pyloric end is rounded. Later, the muscular fatigue gives rise to stasis.

Diagnosis.—1. The cases are found 10 times more frequently in males, usually in the firstborn and healthy at birth.

2. The symptoms commence, not immediately at birth, but after seven days or longer.

3. The vomiting is characteristic, forceful, projectile, after each feeding, and in quantity equal to the previous feeding. It does not contain bile.

4. The infant remains hungry, and often cries out with the hunger or from pain.

5. The stools are not milky.

6. There is visible peristalsis, and the stomach is dilated.

7. A tumor may be palpable.

8. In cases of doubt, the gastric retention test proves obstruction. The technique is as follows: After preliminary lavage, the child is given a measured feeding, and after three hours, the contents are removed by means of a catheter and syringe. If $\frac{2}{3}$ or more is recovered, obstruction is proved.

9. Emaciation is rapid.

Differential Diagnosis.—1. Simple indigestion. There is absence of the above symptom-complex.

2. Pylorospasm: The vomiting is less frequent and less forceful. There is less emaciation and constitutional disturbance, and there may be no tumor.

3. Congenital stenosis or atresia of the duodenum. This may closely simulate pyloric stenosis. The child lives, however, but a very few days, and if life be prolonged, the frequent vomiting immediately after birth takes place, and it is bilious (if the atresia be infrapapillary). There are no stools other than mucus with cellular contents; inanition and wasting progress rapidly. In both conditions there may be dilatation of the stomach, visible peristalsis and even tumor.

4. Malformations of the small intestines.

5. Tumors or enlarged glands near the duodenum, which narrow the lumen through pressure.

Course and Prognosis.—Goldbloom, of Montreal, and Spence made a special study of both types, concluding that in typical severe cases, operation is imperative. They consider that the duration of symptoms prior to operation is probably the most important single factor affecting prognosis. When symptoms have lasted less than four weeks, the mortality is only one-third as great as when four weeks or longer. The mortality is much less in breast-fed babies and in those weighing over 7 pounds; the death-rate increases in direct proportion to the amount of weight lost prior to operation. If left alone, such cases last on an average four days.

Treatment.—In the vast majority of cases, surgical treatment (which in skilled hands is now a simple procedure) is the only suitable method to adopt. For a minority, however, of the mild types, medical measures should, of course, be adopted, but unnecessary delay in a decision may involve the life of the child. In the early stages, when the child is robust, careful medical measures may be tried, with a view to determining if the condition be mild, a mere spasm and temporary obstruction, or a true hypertrophic stenosis. The medical measures are gastric lavage and careful feeding. *Lavage* may be tried, several times daily, the chief factor being its effect in relieving spasm, so that subsequent feeding may pass through. Howland suggested the refeeding of patients immediately after each attack of vomiting, on the basis that spasm is relaxed by the act of vomiting, and food may thus find an exit through the pylorus. His record of cures in mild cases by this method is impressive. *Feeding:* Mother's milk is by far the most satisfactory, but if this be not available, one should use modified milk, with low fat content, or whey, albumin water, and the like. Thick cereals, however, have been highly commended by Sauer, Goldbloom and others, and have been employed successfully in various types of refractory vomiting. Sauer's formula is as follows: Skimmed milk, 9 oz., water, 12 oz., farina, 3 oz., and dextrin maltose, $1\frac{1}{2}$ oz. This mixture is boiled for one hour in a double boiler until too thick to run. Feedings should be given 6 to 7 times daily. The baby is placed on the right side after food Eleven of 12 cases were cured by this method. Saline injections are of doubtful value, though enemata may be necessary.

Atropine Treatment.—It is doubtful if any drug other than atropine is of avail. Haas, writing in 1918, on the "Hypertonic Infant," suggested its relation to stenosis, and that by the use of atropine in doses of 1 drop of a 1 to 1000 solution with each feeding, benefit would result and spasm would be relieved. He further urged the gradual increase of the dose to the point of maximum tolerance. Cures are claimed and perhaps do occur in mild or purely spastic cases. Two objections to this arise. It can hardly be expected that benefit will result where fibrous overgrowth exists, and the delay necessitated by the progressive dosage endangers the chances of recovery if operation is ultimately required.

Surgical Treatment.—The indications are: (1) The definite diagnosis of a severe type; (2) incorrigible vomiting; (3) evidence of obstruction; (4) poor general condition, and (5) absolute constipation. While Holt suggested operation as soon as the diagnosis was made, Thomson decided according to the severity, the effect of diet and lavage, and according to the vomiting and loss of weight.

Operation should never be undertaken as an emergency. There should always be careful preparation of the child, lavage and infusion for days beforehand if at all possible. Poynton suggests giving subcutaneous saline ($1\frac{1}{2}$ ounces) with 2 per cent. glucose twelve hours and two hours before operation. The most important factor in the surgical treatment is the condition of the baby at the time of operation. The earlier, the better, but under favorable conditions, and delay must not be too long in trying out medical measures. When operation is done within a week of the onset of symptoms, the prognosis is excellent.

In view of its simplicity and the success attending it, the Fredet-Rammstedt operation stands alone in the surgical treatment of this malady. The prerequisites to success are gentleness of manipulation, speed, thoroughness of the pyloric incision and a good anesthetist. The pylorus being exposed, is delivered into the abdominal wound, and a longitudinal incision is made extending from the end of the stomach to the end of the pylorus, dividing the hypertrophied muscle (1 to $1\frac{1}{2}$ inches), and then with blunt forceps the edges are divulged until the mucosa is seen and protrudes. This is the complete operation. No sutures are used as a rule. Bleeding is controlled by heat. The pylorus is dropped back into its place, and the external wound is closed. Dangers to avoid are injury to the duodenum and failure to divide all the muscle fibres.

Postoperative care is essential, with special reference to maintaining body heat and proper stimulation, posturing on the right side, mouth feedings as early as possible, enough water, and if need be, subcutaneous saline with 4 per cent. glucose.

Results.—Goldbloom and Spence record 163 cases thus treated, 133 males and 30 females, with excellent results. Under the more favorable conditions, *i. e.*, early operation, good body weight, and in breast-fed children, the mortality was extremely low in comparison with any measure hitherto employed. The operative mortality in breast-fed children was 11.3 per cent.; in those of good body weight, 8.7 per cent.; and when the symptoms had lasted less than four weeks, the mortality was 13 per cent. Poynton, Higgins and Brydson's statistics regarding postoperative mor-

tality are similar: Operations fifty days or longer, 63 per cent. mortality; twenty-five to fifty days, 38.5 per cent. and less than twenty-five days, 6.4 per cent.

Postoperative complications may arise, *e. g.*, shock, hemorrhage (rarely fatal), peritonitis, hyperpyrexia (usually a rise of 102° occurs after operation), and sometimes an infective diarrhœa because of food passing too quickly into the intestine.

CIRRHOSIS OF THE STOMACH

While many authorities, notably Ewing, regard linitis plastica as malignant in character, there are others, more especially Harrigan, Palmer-Watkins and Mills, to whom the condition seems a separate and well-defined disease entity. Ewing holds that although rare cases of ulcer, chronic gastritis, old syphilis, peculiar traumas and atrophying fibrous processes may simulate fibrocarcinoma, yet there is no well-defined group to which a separate clinical picture can be ascribed. He has found every gradation from small-celled diffuse and scirrhus cancer, pronouncedly malignant, to over-cellular granulation tissue containing isolated cells with mucous globules and vascular tissue, with over-growing capillaries suggesting endothelioma. Multiple serositis may account for some forms of this gastric fibrosis.

Definition. *Linitis plastica* in its non-malignant sense, then, may be defined as a non-malignant, slowly developing, and progressive affection of the stomach, characterized by diffuse or circumscribed increase in the connective tissue, involving chiefly the submucosa, and to a less extent the other layers, and sometimes extending to the connective tissue in the parts bordering upon the stomach. The definition in that sense excludes all cases of scirrhus cancer.

Nomenclature. Although the condition has been recognized for more than two centuries, there have been so many views as to its underlying cause and its real nature that the synonyms for the disease are very numerous; *e. g.*, chronic interstitial gastritis; sclerosis of the stomach; fibroid induration; stenosing gastritis (Boas); fusocellular sarcoma (Lyonnet); plastic linitis (Brinton). This last term seems to have been that generally adopted, and certainly the French writers have done much to perpetuate its use. The nomenclature is probably also confused through an apparently unnecessary mingling of various conditions, each of which has a different cause.

Historical. We are indebted to Andral (1835) for the first accurate description of the condition and its differentiation from cancer, though descriptions occur as far back as the seventeenth century. Rokitansky, in 1859, maintained that submucous hypertrophies of the stomach belong in reality to the group of fibroid cancers. Brinton, however, two or three years later, gave to the condition the most used names "cirrhosis of the stomach," and "plastic linitis," thus assuring to it a clinical and anatomical distinctiveness. He classified it, not in the category of gastritis, because he held that the mucous membrane was never affected at the onset, and, indeed, was often quite intact; neither was it a hyper-

trophy, for often in the midst of new tissue much atrophy exists, but rather he regarded it as a cirrhotic inflammation, and not a pure sclerosis, which latter term applies merely to the last stages of the disease. Brinton recognized both its resemblances to and its dissimilarity from cancer, and admitted the difficulty of satisfactory classification.

Among the important papers was that of Hanot and Gombault, in 1882, of special value in view of the careful microscopic examination made in almost serial sections of the diseased tissue. The lesions were most marked at the pylorus and lesser curvature, and there was much invasion of the neighboring tissues, thus creating a callous retroperitonitis; but nowhere could they find either macroscopic or microscopic evidences of a malignant origin. To Bret and Paviot cirrhosis of the stomach is merely a cancer with cells which are metatypical in the stomach, and the real nature of which is only seen in those rare instances where one finds in the generalized process the typical gastric epithelial cells which came originally from the stomach lesion. Garret seemed to regard the condition as of the nature of a fusicellular sarcoma. Jonnesco and Grossman insist on the benign character of the lesions (1908).

Pathogenesis.—Diverse as the views are of the nature of this condition, and uncertain as is still its origin, many of the theories advocated may be readily refuted by an analysis of the reported cases. That it is not essentially an advanced stage of chronic gastritis, is demonstrated by the comparative infrequency of typical inflammatory lesions of the mucosa which in so many cases appears quite unaffected. Alexis Thompson described in 1913, a series of cases with fibromatosis of the gastric wall, non-malignant and not necessarily originating from ulcers. It is, however, more difficult to decide whether the theory of its cancerous origin is or is not applicable to all cases. There is no doubt that clinically the features are, as a rule, not usually identified with cancer of the stomach, *e. g.*, the long duration, the slow cachexia, the long remissions, the character of the emesis, etc.; furthermore, the presence of the oblong tumor, cylindrical, regular, unyielding, with an absence of secondary invasion or metastases, all point to chronic inflammation rather than carcinoma. Ewing's observations, already quoted, seem fairly convincing.

Conclusions from the observations hitherto made would lead one to believe that plastic linitis is an interstitial overgrowth, chiefly in the submucosa, with or without muscular hypertrophy, in some cases primary from an unknown cause, in others secondary, perhaps to ulcer or to cancer, or to a cancerous degeneration of an ulcer; and at times perhaps associated etiologically with other irritating conditions such as might anywhere in the body favor the overgrowth of connective tissue. *Syphilis* seems to be a very definite factor, although in 3 cases described by Faroy with positive Wassermann reactions, the lesions were found to be cancerous. Lossen and Kahl described a case in a child of ten years of age, with congenital lues.

Sex seems to have no influence in its causation. In Lyon's series, there were 23 men and 10 women. *Age* does not seem to be a factor, although it is essentially a disease of adult life. The youngest case reported was thirty-four years; the oldest, seventy-one years. *Trauma*, through

compression of the epigastrium from occupation, is mentioned by Hare, Schacher, and also by Snellen as a possible factor. There is no proof that alcohol induces the linitis.

Pathology.—The lesions which are essentially sclerotic and hypertrophic vary in their location, in the extent and multiplicity of their various foci, and in the degree of invasion of other structures. There are local and diffuse forms, the local chiefly at the pylorus, the diffuse forms extending throughout the body of the stomach. This latter is the type usually described. The stomach itself is either of normal size or contracted. It may be freely movable, fixed in the epigastrium, or pulled up underneath the liver by firm adhesions to the gastrohepatic omentum. While at times it is universally surrounded by adhesions, these are usually most firm at the splenic end. They may be so firm and extensive as to cause intimate attachment to any of the neighboring organs and tissues, to which the same process may likewise extend. The *capacity* of the stomach is usually diminished in these diffuse cases, and it may not contain more than 150 cc. Dilatation occurs, as a rule, only when the pylorus is involved. Externally the organ has a grayish appearance, with a curious opacity due to the overlying peritoneum. It is oval, irregularly ovoid, or cylindrical in shape, resembling in size and form a thickened transverse colon. Its consistency is firm, in parts almost cartilaginous, but with the elasticity and resiliency of a large artery. When removed from the body and placed upon the table its shape is retained because of the thick, firm walls. *The cut surface* is unevenly thick, and may be in some places twenty times greater than normal; although in most instances the average thickness has been 2 to 2.5 cm. Usually the greatest thickness occurs at the pylorus, the hypertrophy gradually diminishing as one gets farther away from the outlet of the stomach. The disease does not extend into the duodenum, a feature regarded as of diagnostic value. More rarely the cardia is chiefly involved, or it may happen that several portions are separately diseased, the intervening tissues remaining comparatively normal. Everywhere the cut surface has a fibrous, pearly grayish appearance and the individual layers of the stomach are readily recognized.

The *mucosa* is often normal in appearance and structure, or slightly thickened and firmer than normal, and in some cases can be lifted off from the submucosa. The thickness is diffuse or patchy, and in a few instances areas of atrophy are also seen, with pale or reddish color or pigmentation. It may be smooth or rough, the surface being sometimes thickly granular with excrescences. Sometimes a few polypi are seen, and there may be erosions, ascribed by Pillet to vascular obliteration due to fibrous constriction. The *submucosa* presents the greatest hypertrophy and thickness. Its tissue is dense and firm, its color grayish-white, and the fibrous strands running through and from it in all directions traverse the underlying muscle tissue so as to form a network about the individual bundles (hence the name "linitis").

The *muscularis* is likewise thickened from true hypertrophy of the muscle, as well as an increase in the connective tissue among its bundles. The fibrous tissue may finally invade even the subserous cellular tissue, so frequently, indeed, that Brinton regarded this layer as the site of

origin. The peritoneum may or may not be involved; in the case of Hanot and Gombault so great was the involvement of peritoneum as to render it worthy of a special title—rétropéritonite calleuse. There was chronic inflammation, with thickening, induration, retraction of the stomach, and fixation of the organ. Amid the adhesions which involve the gastrohepatic omentum, the great omentum, and the gastrosplenic ligament, obliteration of the common duct and the portal vein has occurred, and even an obstructive biliary cirrhosis. The visceral capsules may be thickened (liver and spleen) and these organs themselves sclerosed or atrophied. Even the intestines are sometimes thickened (more especially the transverse colon), and their calibre diminished even to complete obstruction. Simultaneous involvement of the cecum has been mentioned.

The *lymphatics* of the mesentery are frequently seen to be dilated, sometimes so markedly as to suggest that the lymphatic obliteration was the primary cause of the condition (Bouveret, Tourlet). The *glands* are almost invariably small, although their cut surface may show an interstitial increase similar to that seen in the submucosa.

Histology.—The mucosa shows either a normal condition or the minute lesions of a chronic productive or atrophic gastritis. The glandular structures may be displaced and the development of fibrous tissue may cause constrictions and cystic dilatations of the tubules, or else may have caused the gland structures to entirely disappear. In a case mentioned by Osler the mucosa was smooth without any trace of glandular elements—a distinct sclerosis of the mucous membrane itself with atrophy. The lymphoid nodes are sometimes proliferated. The submucosa, which is much thickened by strands of fibrous tissue densely arranged, and forming a network, may be at times most abundantly gathered around the bloodvessels. And the muscularis, which is normal in some places, is in others like an irregular checker-board traversed by intersecting lines of fibrous tissue. The subserous layer exists in various stages of progressive inflammation, and the peritoneum itself may show increased connective tissue.

The *circumscribed form*, of which the commonest and most typical lesion is the "hypertrophic stenosis of the pylorus," shows anatomical lesions of a similar nature, although, as a rule, there is dilatation of the organ rather than contraction, and the muscle tissue itself gradually degenerates. Habershon's fibroid disease of the pylorus and Boas' hypertrophic stenosing gastritis are the synonyms. The delimitation toward the stomach itself is usually gradual, while toward the duodenum it is much more sharply defined. The cases of congenital hypertrophic stenosis of the pylorus may sometimes belong to this category, although their origin is more a developmental morbidity than an inflammation. Of the other sites of localization the cardia has been mentioned, and in Formad's case, in which the greatest thickening was at that orifice, an ulcer existed in the posterior wall near the cardia, the floor of which was formed by splenic tissue and the peritoneal coat of the transverse colon. The stomach was contracted and held less than 150 cc.

Symptoms.—The onset is insidious, and the early development slow, gradual, and by no means easily determined. The early symptoms correspond in most particulars to those of chronic gastritis, and there are vague symptoms of indigestion, with a fickle appetite and usually anorexia, a sense of heaviness after meals, and later vomiting of mucus or of partially digested foodstuffs. In the early stage *pain* is moderate or entirely absent, and rarely so severe as to suggest ulceration. For one or more years these milder symptoms, which are usually slowly progressive, or else with occasional long periods of remission, are gradually superseded by signs that indicate a more serious disease. The pains, which at first were insignificant, become more constant, of a dragging nature, sometimes spontaneous, sometimes only excited by food. They may extend from the epigastrium to the back, and are usually increased by pressure. Nausea, eructations of gas, and vomiting of liquid gastric contents accompany the pain, which is usually relieved by free emesis. The *vomiting*, which is always digestive in time, appears sometimes at once after meals, as though from an involvement of the œsophagus, and Roux has drawn special attention to the diagnostic importance of this symptom as suggesting gastric intolerance because of the rigid contracted cavity. When the chief lesion is at the cardia, regurgitation of food or mucus would be a common sign, but in the commoner diffuse cases the vomiting appears one to two hours after meals. It is most continuous in the severe cases, and if stenosis of the pylorus be present there will be signs of retention. In about 20 per cent. of the cases slight hematemesis is noted, but there is never much bleeding because there is rarely ulceration. For the same reason obvious melena is uncommon. The increasing limited capacity of the stomach for food is an important symptom. The intestines are not commonly involved, but sometimes the bowels are irregular and there may be a mucous enteritis. The general appearance of the patients may vary; while, as a rule, some pallor is conspicuous, the patient has lost flesh, and has become somewhat cachectic, yet at other times, both the nutrition and the color are well preserved, to which Trousseau drew special attention.

In the gastric contents, the HCl is variable, often absent, and lactic acid is commonly present. The roentgen-ray examination reveals a small stomach, often with a patent pylorus of the diffused type.

Examination of the abdomen in uncomplicated cases may show some retraction of the epigastrium, or a mass, more or less localized, may be seen prominently beneath the abdominal wall or moving with respiration. Peristalsis may be visible. Palpation demonstrates, usually, a diffuse resistance in the epigastrium, not always marked, especially if the contracted stomach be drawn up and fixed beneath the liver. At other times a hard oblong transverse tumor may be felt in the epigastrium, and extending to the left false ribs, or again only in the neighborhood of the pylorus. The *mobility* of the tumor varies according to its site and the nature and extent of any adhesion present. It has been mistaken for a movable spleen and for the transverse colon. Trousseau has drawn attention to the sensation of grating conveyed to the palpating hand on deep respiration. As time progresses, the condition may extend

beyond the stomach to the peritoneum and the surrounding viscera. Ascites may develop, make palpation difficult, and conceal the real underlying cause; or the symptoms may change to those of intestinal obstruction, in which to the conditions of cachexia and anasarca may be added persistent and uncontrollable vomiting until death follows from asthenia. Jaundice is rare in these cases, and apparently due only to constriction of the common bile duct from adhesions. When the cardiac orifice is mainly involved, so that constriction occurs, the process is more rapid and the fatal termination induced through starvation and inanition. Rapid emaciation, dysphagia, regurgitation of mucus and food are the characteristic features. When typical hypertrophic stenosis of the pylorus is present the signs are those of a benign stenosis. To the primary digestive symptoms are added the slow development of the affection, the marked emesis, with is digestive, infrequent, and small in amount at first, and later less often but more abundant; later come the signs of marked motor insufficiency with constipation, great thirst, and hunger, diminution in the quantity of urine, localized pain, visible peristalsis, perhaps a visible tumor, rapid emaciation, and death from inanition.

Course.—*Chronicity* is the characteristic feature, and although Bouveret's case lasted apparently only twenty months from the onset, this is much shorter than the average duration. Tourlet's patient suffered seven to eight years before operation, and the average is perhaps ten to fifteen years. The average duration in Lyons' series was twenty-three months. No general rule can be made, for the duration depends on the variety of the lesion. Circumscribed cases not obstructing an orifice last much longer than those which are localized at the pylorus, or still shorter time if at the cardia. The diffuse cases will be of still shorter duration than those confined to the pylorus, and when peritonitis, ascites, and adhesions supervene, the course is rapidly downward.

Diagnosis.—This has rarely been made during life. Six of Lyons' cases were diagnosed as non-malignant, although after death, a microscopic examination revealed small-celled cancer in all. An operative diagnosis was made on 5 others, though the microscopic examination revealed again other lesions, in one, adeno-carcinoma; in one, a colloid cancer; in another, lues; in yet another, simple ulcer; and in the fifth, an unaccountable simple hypertrophy. When, even at autopsy, it is so difficult to make an anatomical diagnosis, one can scarcely expect that the clinical diagnosis would be easy. While the uncomplicated cases are difficult to determine, still more do the cases with complications lack ready means of diagnosis. The chief features are the long duration, the slow cachexia, the limited capacity of the stomach, and its intolerance of much food at any one time, the absence of hematemesis or melena, the presence of an oblong cylindrical tumor in the epigastrium in patients in whom the history and physical signs present neither the local evidence of carcinoma, metastases, or any signs of generalization. Plastic linitis has frequently been mistaken for cancer of the stomach, for portal cirrhosis, obstructive biliary cirrhosis and simple chronic or tuberculous peritonitis. When pyloric stenosis is present one considers the possible presence

of an old gastric ulcer and consequent perigastritis, and for the elucidation one trusts to the past history. Syphilis rarely presents similar symptoms; as a rule, the lesion presents mere strands of fibrous tissue, and gummata are uncommon. The roentgen-ray findings show a small irregular lumen, with contraction of the lower portion. If a filling defect exists, the inner margin is smooth. Deguy, in 1896, described his case in which, for the first time, a diagnosis was made during life, and subsequently confirmed at autopsy. McCrae reported a similar experience from Osler's clinic.

Treatment.—The rational treatment is essentially surgical. Medically there are but two considerations: in the early stage to treat the condition as in chronic gastritis, and later, when stenosis exists, to employ palliative treatment until the more radical cure is attempted by surgical measures. Gastro-enterostomy as a mere palliative operation has been found successful, but where possible, a removal of the diseased tissue, in view of the possible cancerous nature of the affection, is the one thoroughly scientific treatment worthy of consideration—for the localized condition, pylorectomy, and for the diffuse lesion, total resection. Mauclaire and also Terrier recorded cases in which an apparent cure followed exploratory laparotomy, and Roux records an interesting case in which the patient was well three and one-half years after operation (anterior gastro-enterostomy). Total resection was performed by Gayet and Patel (1904) for a linitis of definite malignant origin, this being probably the first operation of its kind for this condition.

HEMATEMESIS

Definition.—Hematemesis is a vomiting of blood—regardless of its origin—and it must not be confounded with "gastrorrhagia," for the blood vomited in hematemesis may come from other sources than the stomach itself. It is merely a symptom, to be referred not only to the stomach itself, but also possibly to conditions in structures contiguous to that organ. It is much more common than is usually recognized, probably because spectroscopic, microscopic, or chemical aids are not usually employed to reveal the presence of blood when not in macroscopic quantity. Certain minute hemorrhages more often go unrecognized than is usually believed.

There may be no anatomical lesions (diapedesis), as in Lancereaux's supposed neuropathic hemorrhage occurring in gouty, nervous, or rheumatic individuals; or the lesion may be so minute as to escape detection even although the hemorrhage be very copious. Such conditions often arise from a general oozing from various portions of the mucous membrane, and in some cases the blood streams forth from a wide surface of the mucosa. More often the lesion is obvious (rhexis), and a gross lesion, such as ulcer or cancer, explains its origin.

Etiology.—The bleeding may be (1) gastric, or (2) extragastric.

1. **Gastric Bleeding.**—Gastric bleeding may be from *local* or *general causes*. *Local causes* may be *direct* or *indirect*.

Direct Local Causes.—Among these are: Ulcers simple, round, tuberculous, typhoidal, diphtheritic, septic, etc.; varices, and miliary aneurisms, perhaps associated with arteriosclerosis; gastritis, simple, acute, chronic, phlegmonous, or toxic; cancer and trauma. The trauma may be direct or indirect, and the causes physical and chemical. Physical causes, *e. g.*, foreign bodies; the strain of vomiting; injury from the stomach tube; stretching from distension by CO_2. Chemical causes, as poisons, purgatives, emetics with degeneration of the mucous membrane, fatty, hyaline, or amyloid; and postoperative hematemesis.

Indirect Local Causes.—Portal obstruction in cirrhosis of the liver, syphilis of the liver, atrophy, pressure on the portal vein, portal thrombosis (of these cases 80 per cent. are œsophageal in origin). Diseases of the spleen, especially splenic anemia. Thoracic disease with circulatory obstruction, emphysema, fibroid lung and organic heart disease.

General Causes.—In these hemorrhage occurs from various mucous membranes as well as from the gastric. The conditions are many: sepsis (with or without signs of local lesion); the exanthemata (hemorrhagic forms) and other fevers such as typhoid; hematemesis neonatorum perhaps belongs to this group; autotoxic states, uremia, cholemia, etc.; blood dyscrasias and diseases, hemophilia, purpura, scurvy, pernicious anemia, leukemia, etc., possibly degeneration of vessels and capillaries, or emboli with hemorrhagic infarctions or infected thrombi; neuropathies, epilepsy, tabes, general paresis, hysteria, and meningitis, in all of which the hemorrhages may be vasomotor in origin; vicarious menstruation and burns. Debove and Coutois-Suffit attribute these unexplained hemorrhages without discernible lesions to abdominal congestion due to depressor nerves acting on arterial tension, as has been declared possible by Ludwig and Cyon.

2. **Extragastric Bleeding.**—Apart from the hemorrhages which arise in the œsophagus from varices, etc., the blood may come from abscesses contiguous to the stomach bursting into that organ; or ulcers and fistulæ may open up a suppurating tract into the stomach and cause hematemesis. Vertebral caries or aneurism of the abdominal aorta or cœliac axis may perforate the stomach and cause hematemesis.

Age and Sex.—The age at which hematemesis occurs is usually from fifteen to forty; it is rare in infants. It is more common in women.

Pathology.—The originating cause will in large part determine the nature of the general changes, *e. g.*, cachexia in cancer, cloudy swelling in sepsis, etc. The mucous membrane of the gastro-intestinal tract is usually pale, and about the seat of the hemorrhage there will be the remains of blood more or less tarry. The clot formed varies in appearance. If there be little blood and gradual oozing one gets a chocolate or coffee-ground appearance perhaps, with black specks like powder sprinkled through the contents, or a diffuse bloody, or darkly stained fluid. At the seat of the hemorrhage one may find eroded vessels, and sometimes an imperfect clot formation. The opening is often very difficult or impossible to find or only evident after injection from the main vessels.

Symptoms.—These depend chiefly on the amount of blood poured out and the rapidity with which it flows. Sometimes gastric hemorrhage is

latent, especially when the amount is small, and the blood must then be detected in the vomitus or feces (occult). At other times the blood is not vomited even when very copious, and the patient may even die with no other signs than those of internal hemorrhage. In true hematemesis the blood, however, is vomited and may be large (up to two liters) or small in quantity. When small in amount it is usually mixed with mucus and food and appears either as minute specks or as streaks mixed with the other gastric contents. Its color depends upon its amount and the time in the stomach. The blood of minute hemorrhages is most easily transformed in color. When fresh, the color is bright and the blood cells are unchanged. When for some time in the stomach, the blood is dark resembling coffee-grounds. If 50 cc. of blood reach the stomach and remain in it for five minutes, the red cells become altered and the color already much darker than normal. Microscopically one sees cells more or less broken down and blood pigment. Sometimes, again, there is much dark-red clot with an acid reaction.

The patient may have a sense of warmth in the epigastrium and along the œsophagus; sometimes an abnormal pulsation with fulness is felt in the abdomen. Pain is frequently felt in the epigastrium for some time before hemorrhage, and may cease when this occurs. If quickly vomited, the blood may come not only through the mouth, but from the nose, and may get into the air passages and cause coughing. As a rule, hematemesis is accompanied by great anxiety and fear of death. The general signs of hemorrhage are present—pallor, faintness, dizziness, ringing in the ears, specks before the eyes, dimness of vision, cramps in the thighs and calves and perhaps clonic spasms, œdematous swellings over the smaller bones and eyelids, drowsiness, insomnia at night; the pulse is often dicrotic, anemic systolic murmurs are heard over the heart, and a venous hum over the large vessels. The blood picture is that of a secondary anemia. Fever is present, especially if the intestines have contained much blood, because absorption occurs; on this account the temperature is not infrequently reduced by purgative treatment. Recovery is sometimes rapid, at other times very slow, because bleeding from the vessels may be often repeated and small in quantity.

Diagnosis.—When hematemesis has occurred one must consider the following questions: (1) Does the vomitus really contain blood? (2) If so, is it from the digestive tract? (3) Is it gastric in origin, and if so, does it come from near the cardiac end, from the duodenum, or from the stomach proper? (4) What is the etiological and anatomical lesion? (5) What vessel is affected? (6) Is it amenable to medical treatment, or, if not, is it accessible to operation?

Hematemesis is so often latent or unrecognized that one must make careful observations both as regards the previous gastric history and the present state of the abdomen and gastric contents or vomitus. Not infrequently there is a fulminating gastrorrhagia, in which no blood is vomited and the diagnosis is made from the general sensations and symptoms of hemorrhage and the previous history of gastric disease. Even when very copious it may not be evacuated and the patient may

die with merely the signs of internal hemorrhage, or vomiting may be delayed for some time, or the blood may appear only in the stools.

1. *Is Blood Present?*—It may happen that a faulty diagnosis is made because the food previously taken may resemble blood, *e. g.*, red wine, cherries, cranberries, red cabbage, red turnips, red sausages, coffee, and cinnamon. Pseudohematemesis may be associated with various preparations of iron or bismuth; the bismuth crystals, moreover, under the microscope, resemble to some extent those of hematin. In doubtful cases one should always examine microscopically for blood cells or blood pigment, and where doubt still exists, test with the spectroscope or by chemical means, to prove the presence of blood.

2. *Is the Blood from the Digestive Tract?*—The blood may not be from the digestive tract at all, but from hemoptysis, epistaxis, or from a ruptured aneurism. To differentiate from hemoptysis one must remember that in hematemesis the blood is dark-red in color, usually resembling venous blood; that it contains no air, has usually an acid reaction from contact with the gastric juice; that it is mixed with food; that it is vomited, not coughed; and it does not contain tubercle bacilli, for tuberculous ulcers of the stomach are extremely rare; and lastly, local findings in the lungs are absent, while those in the stomach are often obvious; or there may be signs of a heart lesion, the possible cause of hemorrhagic infarction of the lungs. Epistaxis may give rise to error through swallowing of the blood and subsequent vomiting. For this reason it is always well to examine the nasal cavity carefully.

3. Having excluded other sources, one must decide *whether the hemorrhage be gastric, duodenal, or œsophageal.*

Œsophageal Varices.—There is nothing distinctive about the hemorrhages from the œsophagus. Œsophageal varices are most commonly associated with early cirrhosis of the liver, and one should therefore examine carefully for it. The evolution of the condition may help the diagnosis. In two-thirds of such œsophageal hemorrhages the patient improves, but recurrence takes place after intervals of days, months, or years. Sometimes they are fulminating in character. Sometimes the cirrhotic changes in the liver are very slight, and a toxic agent is suspected. It is in cases such as these that some outside agency is the main factor, *e. g.*, the spleen. Apart from gastric ulcer and hepatic cirrhosis and the leukemias, the most important causative agent is splenic disease, all the more important because of the therapeutic possibilities with reference to splenectomy. *Œsophageal cancer* may also simulate gastric ulcer, but has other evidences of malignant disease. *Œsophageal ulcer* causes pain after swallowing, increased secretion and regurgitation of mucus and food, and progressive signs of stricture.

Duodenal hemorrhage from ulcer is sometimes accompanied by hematemesis. Men are more commonly afflicted. As a rule, the stools show the first evidence of this condition. The pain is usually situated more to the right; it occurs later after meals than does that of ordinary gastric ulcer (two to four hours) or, at all events, is increased at that time; the digestive signs of pain, etc., coming on several hours after meals and the presence of HCl help to establish the diagnosis.

4. *The nature of the causative lesion* is often most difficult to determine, and is sometimes impossible. *Neuropathic hematemesis* is a problematical condition which is receiving less recognition each year.

Vicarious hemorrhages usually occur in the absence of any gastric signs, have more or less periodicity, and at best are quite rare. They occur either at the time of the menses, or at times quite apart from that period. The menses may be absent and replaced by the hematemesis, the latter may coincide, with diminished menstrual flow. Legroux had a patient in whom monthly hematemesis occurred during the first seven months of pregnancy.

Varices in the stomach are very rare, and doubtless have the same causes as those in the œsophagus.

Venous Stasis.—Although varices are rare, dilatation of veins is common, and a rupture of the capillaries of the mucous membrane frequently occurs, as in cirrhosis of the liver, inflammation or tumors of the pancreas, cancer of the gall-bladder, wounds in the vicinity, etc. In the vomitus of peritonitis and intestinal obstruction there may be a little showing of blood; perhaps these types are infectious in nature.

Hemorrhagic Erosions.—These show only bleeding and few or no other symptoms. Often the blood is found only in the washings from the empty stomach and usually then associated with chronic gastritis. The bleeding may occur by the mouth or the rectum, as in latent ulcers. Such cases are rarely fatal, and usually occur in men who are in poor condition, with advanced tuberculosis, or alcoholics with cirrhosis, etc. C. H. Miller attributes many gastric hemorrhages to erosions from swollen or ruptured lymphoid follicles in the stomach mucosa which has become thinned, while the basement membrane is unusually thickened. Thus the follicles are less covered, and under abnormal conditions, many lymphoid follicles become swollen, disintegrated, and softened. They in this way reach the surface, and may burst through the mucosa, thus leaving the basement membrane temporarily exposed to the gastric juice, which digests some of the numerous vessels of the submucosa.

Miliary aneurisms of the submucous arteries as a part of generalized aneurisms cannot be distinguished clinically.

Simple Ulcer of the Stomach.—Hematemesis coming on in healthy individuals or in those who have suffered from stomach disorders is due in the majority of cases to ulcer in some stage. The history with the symptom complex, the oft-recurring hemorrhage in youthful subjects with good appetites and good albumin digestion, the presence of HCl in the contents, and the absence of cachexia aid in determining the presence of ulcer. The important point is not so much the exact diagnosis of the lesion, as of the value and possible success of intervention.

Cancer of the stomach is usually easy to diagnose from the history and the findings. The patient is older, with anemia, perhaps cachexia, anorexia, no HCl in the contents, but lactic acid instead, etc. While sometimes hemorrhage in cancer is acute and fatal, as a rule, bleeding is small, recurrent, and of a coffee-ground appearance. Occult blood in the stools is much more constant. However, many exceptions occur, and all possible factors must be considered together.

6. *Are the Ulcer and Vessel Accessible for Operation?*—Fresh ulcers usually erode the superficial vessels in the wall and are readily reached; old ulcers may be adherent to the pancreas and liver and are sometimes hollowed out. Adhesions form beyond the limits of the organ and are deeply situated, fixed in immobile tissues, perhaps hard or friable, the vessels are deeper, less accessible, and often larger. In a word, they erode rather the extrinsic arteries, such as the splenic, and make operation difficult, perhaps impossible.

Prognosis.—This depends chiefly upon the cause and, to a less degree, upon the severity of the hemorrhage. In serious general conditions hematemesis is one of the worst prognostic symptoms. When blood flows from outside structures into the stomach the prognosis is bad. In poisoning cases the amount of hemorrhage itself is of no prognostic importance unless the contents be putrid, in which case deep ulceration may be suspected and death may follow from sepsis or perforation. It is often difficult to differentiate between rupture of the small and the large vessels, and statistics vary very much because there is nothing in the evolution of the condition or in the antecedent hemorrhage which can prognosticate a recurrence or progressive gravity or origin; one cannot say from the amount of blood and the area of pain what vessel is affected or whether the hemorrhage will recur. The most copious hemorrhages may have no visible anatomical lesions of the mucosa. Large hemorrhages, however, are rarely fatal (3 to 4 per cent., Lebert).

Sometimes in gastric ulcer hemorrhage causes cessation of all the other signs; in cirrhosis of the liver that organ diminishes in size after a hematemesis. The cause is often more serious than the hemorrhage itself. In ulceration the prognosis is difficult to determine. Hyperacidity after the hemorrhage may act as an irritant and cause renewed ulceration and bleeding. For one month after a severe hemorrhage the condition continues serious, but from that time onward becomes less so, so far as life is concerned, but there is always the same uncertainty as regards recurrence. After eight to ten days the prognosis may be given as good, because of thrombus formation, although one must always keep in mind the possibility of hemorrhage from another part of the ulcer where a newly attacked vessel has opened. In cancer, hematemesis may usually be considered as a fatal sign because indicating advanced disease, although exceptions occur with bleeding at an early stage.

Preble concludes, from an analysis of 60 fatal cases of hematemesis with subsequent autopsies, that: (1) While not rare, fatal hemorrhage is at all events not common in cirrhosis of the liver. (2) The first hemorrhage in cirrhosis is fatal in only one-third of all cases. (3) Œsophageal varices are the source of the bleeding in 80 per cent. of cases; in half of these, ruptures were found and are probably much more common than is generally realized. (4) Fatal hemorrhages sometimes occur from invisible ruptures of numerous capillaries of the gastric mucous membrane, and, as a rule, there are some accompanying signs of early cirrhosis of the liver.

Treatment.—The indications are as follows: (1) Prophylaxis, when the possibilities of hematemesis are recognized. (2) Discovery of the

etiological factor. (3) Control of the hemorrhage as quickly as possible. (4) Prevention of its recurrence. (5) Prevention of injurious sequelæ.

Prophylaxis depends upon the discovery of the possible underlying condition and its judicious treatment. Control of the hemorrhage requires *rest* in general and of the stomach in particular. The patient should be put to bed with the head low and kept as quiet as possible. All tight clothing should be removed and the patient encouraged with the explanation that hematemesis of itself is of no very serious import. Should faintness supervene, the face should be sprinkled with cold water, ammonia placed beneath the nostrils and if necessary camphor oil, ether, or caffeine, given hypodermically; a hot bottle may be placed to the feet. Morphine should be given promptly, and in certain types, transfusion should be done, in order that the blood loss may be restored and the clotting elements increased. This is applicable more especially to the small repeated hemorrhages rather than to the larger one, or in cases in which operation has already controlled the source of bleeding; or again, as a preparation for operation. It does not seem that transfusion is ever so useful or so safe in copious bleedings from large vessels. Where after a preliminary hemorrhage without ulcer, a second one follows in a few days, an emergency operation must be done to save life. In ulcer, the inadvisability of operation during hemorrhage is agreed upon by most clinicians, chiefly because of the poor state of the patient, the doubt in the diagnosis, and because recovery without operation is the rule. Finsterer however, advocates prompt operation when hemorrhage occurs. He reports a mortality of 5.5 per cent. in this way, whereas where the interval between the hemorrhage and the operation was longer than forty-eight hours, the mortality was 49 per cent. An ice-bag may be suspended from a cradle so that it will come into gentle contact with the epigastrium. All food should be stopped for three days and the patient allowed only some ice to suck, but not to swallow. After three days, glucose enemata may be given, three times daily. No food should be given by mouth until after the first week, and then, only gradually, boiled milk, broth, or gruel.

Lavage of the stomach is best avoided, so, too, all local hemostatics. General hemostatics are perhaps beneficial; epinephrine, in doses of 25 drops of the 1 to 1000 solution by mouth daily has apparently been of service. One may use rectal injections of calcium chloride, 4 to 8 gm. (℥j to ℥ij) daily. The reflex effect of heat as administered by hot rectal injections (115°) has been much recommended.

Accessory Treatment.—Cold water enemata are useful for retained blood in the bowel. For the anemia, which may persist, one should give good food, and iron if the patient bears it well.

Surgical Interference.—*Indications.*—The blood count and estimation of hemoglobin *per se* are of little value. Appreciation of the general condition is more important than an estimate of the hematological state. If a low blood count has supervened on a previous anemia the condition is more grave. The pulse has doubtful value. The amount of hemorrhage is also of little importance as compared with its recurrence, which implies an end to medical treatment. For general surgical indications see the section on the Treatment of Gastric Ulcer.

SYPHILIS OF THE STOMACH

Attention has been drawn to this subject for some years, more particularly since the publication by Chiari (1891), discussing 98 cases, many of which, however, were of very doubtful origin. Myers, in 1912, recorded 58 cases, since which time many writers have made important contributions. Brams and Bloch reviewed 142 cases.

In the light of our present knowledge, it is extremely unlikely that the large numbers of cases recorded by some writers are trustworthy; indeed, it is held by various authors that the number of authentic cases recorded is but 20 or 30. The bibliography on the subject is dealt with by Brams and Myers.[1] The former holds that up to 1924 only 17 cases are recorded in which the anatomical description is sufficiently complete to diagnose gastric syphilis. The statistics as to the incidence of syphilis become valueless unless sufficient evidence is given as to its occurrence. Eustermann's statistics show only 0.3 per cent. in 2500 cases operated upon, and T. R. Brown estimates that there is at most only 1 case in every 100 organic lesions of the stomach. Gatewood regards it as much more uncommon, finding only 3 instances out of 483 gastric and duodenal ulcers. Only such ulcers may be regarded as syphilitic as are the result of degeneration of a gumma.

This evidence cannot be based merely on the presence of gastric symptoms with a positive Wassermann reaction or even gastric crises. Patients may have a simple ulcer of the stomach with a positive Wassermann reaction, and the two conditions may be quite dissociated. On the other hand, a condition resembling syphilis of the stomach at operation may be in a patient with a negative Wassermann reaction, so that to identify the case as one of gastric syphilis, a combination of all the features of the diagnosis must be assembled. This would include the following: (1) A positive Wassermann reaction. (2) Evidence either by roentgen-ray, operation or autopsy of an anatomical lesion characteristic of syphilis. (3) The therapeutic test by means of which an existing syphilitic lesion is cured by appropriate procedure. Congenital syphilis of the stomach has probably been found in a few cases, and is a lesion that one may expect to find, though rarely. As a rule, syphilis of the stomach is acquired.

The Lesions.—These are essentially tertiary, although secondary lesions may, and no doubt sometimes do occur, producing ordinary signs of indigestion such as one finds in various mild organic diseases of the organ. The two main lesions described are as follows: (1) *Gumma.* This occurs with or without ulceration, is rarely large, and is usually situated at the pylorus or at the lesser curvature, more rarely at the cardia. These gummatous ulcers are usually accompanied by perigastric adhesions and a proliferative hyperplasia of the gastric wall. The lesions are often multiple, and occur either as broken-down gummata or as focal necroses from anemia. Ulcers of this kind are usually shallow, seldom extend beyond the submucosa, and are irregular in outline. (2) A *diffuse infiltration,* more often in the middle of the stomach, causing a widespread thickening of the wall, and more or less retraction or contraction of the viscus. These infiltrated areas may be accompanied by shallow, serpigi-

[1] *Jour. Surg., Gyn., and Pediat.*, August 23, 1923.

nous ulceration, and indeed, an ulcer on a widespread area or infiltrated base is rather characteristic of the syphilitic process. The process begins in the neighborhood of the muscularis mucosa: there is proliferation of connective tissue of the submucosa, with abundant granulation tissue and many plasma cells in the mucosa and internal layer of submucosa.

The *histological* changes are briefly: Thickening of the submucosa, perivascular infiltration, panarteritis, panphlebitis, and a diffuse lymphocytic infiltrate. Three types are described: (*i*) Endarteritis obliterans with periarteritis and small-celled infiltration. (*ii*) Gumma with plasma-cell granuloma growing out of a diffuse gastritis. (*iii*) Sclerogummatous lesions of perivascular origin in the submucosa, with infiltration, inflammation and proliferation.

The microscopic lesions are quite unlike those of ulcer or cancer. The mucous membrane is atrophied where the lesion occurs, due no doubt to defective blood supply through obliteration of vessels. The muscularis is thickened and dense with fibrosis; the submucosa is hypertrophied, thickened and fibrosed. While these appearances suggest linitis plastica, there is more evidence of obliterative endarteritis. The pronounced œdematous swelling of the serosa, with the other inflammatory signs, leave a very characteristic impression.

The *sequelæ* of the original lesions include perigastric adhesions, various deformities (the most common, hour-glass contraction), pyloric thickenings, etc. Deformities always occur because of the multiple scarring ulcers, the areas of infiltration and the perigastric adhesions. The size of the stomach is always diminished and the wall is thickened.

Site.—The gummatous lesions usually occur at the pylorus or lesser curvature, more rarely at the cardia, and sometimes up along both curvatures to the œsophagus. The infiltrating lesions are often hard to distinguish from scirrhus of the stomach, from linitis plastica or from a sclerotic ulcer of simple origin.

The spirochetes are conspicuous by their absence in acquired cases.

Sex.—Males preponderate (74 per cent.).

Age.—The average age is thirty-five years. Authentic cases have been described at various ages from twenty to fifty-seven. A positive Wassermann was obtained in 75 per cent. of cases.

Symptoms.—The onset of symptoms is on an average eleven years after infection. Cases are reported which occurred after one year and others which gave symptoms only after twenty-eight years. The *duration* of the symptoms is from seven months to seven years, the average being about three years, though this, of course, depends on the type of the anatomical lesion and the treatment given.

The symptoms are characterized by their irregular atypical occurrence. The disturbances of digestion are unusual and varied. It is noteworthy, however, that symptoms often occur only later on in the disease, *i. e.*, after great morbid changes have already occurred in the stomach. *Pain* is one of the most constant symptoms. It is usually in the epigastrium, but varies much in situation and extent, sometimes radiating to the back. It occurs generally after meals, but is sometimes nocturnal and varies greatly in degree. It is a disputed point as to whether or not gastric crises are not really a syphilitic lesion of the stomach.

Bouchet and Lamy described 8 cases of gastric radiculitis with definite nerve lesions all due to syphilis. *Anorexia* as a symptom of gastric syphilis has been emphasized by Galloway. Flatulence and constipation depend entirely upon the nature of the lesion present. Vomiting occurs in 75 per cent. of the cases, and usually relieves the pain. The type of vomiting depends entirely on the stage of the disease, the kind of deformity produced, the patulousness of the orifice and the degree of stasis. *Hematemesis* is considered by Eustermann as rare, while Brams, on the other hand, noted it in 40 per cent. of his cases and says it is often profuse.

Emaciation is always present, though the loss of flesh is never so great as in malignant disease, nor is the obvious cachexia of cancer evident. The physical examination is often negative. Comparatively rarely does one feel a mass due to a gumma, and only occasionally does infiltration of the gastric wall render the tumor or ridge palpable. This, indeed, is considered one of the characteristic features. The liver is sometimes enlarged and smooth, so also the spleen. The Wassermann reaction is positive, but often a provocative injection is necessary to induce it.

Gastric Analysis.—The presence of achylia in 82 per cent. of cases and of subacidity in 72 per cent. indicates how frequently this condition is present, and according to many observers, is one of the striking proofs of the probable existence of syphilis. Hypersecretion does not usually occur and lactic acid is only present where there is marked retention. *Occult blood* has been found in 17 per cent. of cases and blood is present in the gastric contents in 25 per cent. Records indicate that in the secondary stage of general syphilis, the subacidity is a common finding, while in the tertiary stage, achylia is extremely frequent.

Roentgen-ray Examination.—The signs may be classified according as there is: (1) A simple gummatous ulceration. (2) A gummatous tumor (tumefactive). (3) An extensive induration (linitis plastica). (4) Pyloric stenosis. While there is nothing pathognomonic in the radiological picture, certain striking features are worthy of mention. By means of the screen, one may see a fixation of the midportion of the stomach from general infiltration and sometimes a bilateral hour-glass stomach. The condition is suggestive of gastric lues, all the more so if there be absence of cachexia, if no mass be palpable, and if there is evidence of lues elsewhere. Dumb-bell contraction of the stomach often occurs with dilatation, but there may be no incisura, crater or perforation. If there be massive filling defects, they are the result of shrinkage of the stomach.

Filling defects occur sometimes, and usually show a broad surface. In many cases the filling defect is at the pylorus and usually such findings are indistinguishable from cancer, so far as the radiological picture is concerned. Peristalsis is atypical. The six-hour residue may be present or there may be incompetence of the pylorus from the stiffened stomach. The lumen of the stomach is small.

Diagnosis.—This is not based on any one finding but on the history and clinical and roentgen-ray signs combined with a positive serological test and therapeutic results. The history must be not only of the infection but of the chronic course of the disease, with its capricious development, its atypical symptoms and its rebellion to the usual courses of

treatment. Fenwick considers that in luetic cases there are greater pain and vomiting than in ulcer, but less hemorrhage; and further, that the symptoms show a much greater tendency to relapse. The failure to find a palpable mass, while the roentgen-rays indicate an extensive involvement, suggests the presence of syphilitic lesions. The presence of achylia or subacidity, combined with the syndrome of benign ulcer or malignant disease, is also suggestive. The patient is usually younger than the age for malignancy, and while there is some falling off in general health, there is no cachexia. The positive Wassermann reaction does not necessarily mean that the lesion is in the stomach. The course is less rapid and less continuous than in cancer. The roentgen-rays may show a fixation in the body of the stomach, often with incompetence of the orifices, diminished capacity of the stomach, as well as of motility, the picture resembling that of linitis plastica. *The symptoms are insignificant as compared to the degree of anatomical involvement.*

The **course** of the disease varies. It is progressive in 90 per cent. and there are but few records of conspicuous cure. Death occurs on the average between one to three years.

Treatment.—Whenever in a chronic gastric ulcer, without much deformity, ordinary methods of treatment have failed, one should always carry out anti-syphilitic treatment before operation is attempted. Good results have been obtained in the exudative stage by medication and the treatment should be short and intensive. Quite a few cases are recorded in which chronic ulcers, with much fibrosis, have been healed by anti-syphilitic treatment. C. B. Keenan, of Montreal, has stressed the importance of this means of treatment in chronic duodenal ulcers in particular, having successfully treated some chronic gastric and duodenal ulcers by mercury and iodide. In one of Bram's cases, with a negative Wassermann reaction, cancer had been suspected, but a complete cure was obtained by means of antisyphilitic treatment. There seems little doubt that in the early stages of many doubtful organic diseases of the stomach, anti-syphilitic treatment is of benefit. When dense fibrous scars have formed, as the lesion becomes more chronic, one cannot expect much benefit. In some of these older cases, however, there are concomitant lesions of a subacute type which may be benefited and thus give a partial relief to the general digestive symptoms. Where deformities exist, surgical measures should be adopted if, after intensive treatment, benefit does not accrue. Preparations of arsenic should be used, and mercury by inunction or intramuscularly. Iodide should be given persistently.

The diet must be governed according to the presence of open ulcers or to disturbance of the motility. Soft foods, with sufficient caloric value, should be given, and any solids should be administered in a digestible form. Lavage should be carried out with care, and only when the disturbance of motility indicates its need. For the achylia, HCl, is often beneficial, and iron for the anemia. Bouchet recommends the destruction of the nerve roots or extraction of the intercostal nerves, when evidences exist of an obstinate radiculitis. Thomsen records a cure of gastric crises by left vagotomy. The indications for surgical intervention are: (1) Acute complications (perforation, etc.). (2) Final stages of healing (*i. e.*, the results of cicatrization, with deformities, stenosis, hour-glass and adhesions). E. Graham mentions 34 cases of pyloric resection, including 2 of his own, with good results.

CHAPTER X

DISEASES OF THE INTESTINES

By ALFRED STENGEL, M.D.

PHYSIOLOGY OF THE INTESTINAL TRACT

Motor Function of the Intestines.—The movements of the intestines serve three important purposes: (1) The onward movement of the contents; (2) thorough mixture of the chyme with the digestive secretion and close contact of the contents with the absorptive mucous membrane; (3) the propulsion of the venous blood and chyle away from the bowel. The old idea that the purpose of intestinal movements is to cause the passage of the intestinal contents toward the rectum has been disproved by investigations which show that certain conspicuous movements of the bowel thoroughly churn the contents and thus mix the chyme and the digestive fluids and at the same time bring the contents of the bowel into more complete contact with the mucous membrane.

Three chief forms of movement are recognized: (1) Peristalsis proper; (2) rhythmic segmentation; (3) antiperistalsis.

Peristalsis Proper.—Peristalsis proper, or the movement that causes the forward flow of the bowel contents, is a wave-like contraction that runs for some distance, gradually diminishing toward the end of its course, where a new wave starts up. The bowel contracts behind the contents and relaxes in front of them (Starling). These movements vary in rapidity and strength normally, and may become excessive in pathological states. Violent stimulation may cause a tonic contraction of a segment or a considerable portion of the bowel. The peristalsis of the colon causes an alternate protrusion and retraction of the haustra.

Rhythmic Segmentation.—In skiagraphic studies of the movements of the intestinal contents Cannon found that constrictions occur at various places, and the portions of the bowel between the constrictions may subdivide by secondary segmentation. The segments subsequently reunite and divide with renewed contractions. As many as thirty segmentations a minute were observed. These segmentations involve the contents of the bowel and do not indicate the kind of contractions that occur in the wall between the segments. Possibly the swaying movements or waving movements described by Raiser may be the occasion of the segmentation. These are backward and forward contractions and relaxations affecting a limited part of the bowel and running in a direction parallel to its length. There is no appreciable narrowing of the lumen of the bowel. Such contractions might very readily divide the contents of the bowel into segments. Rhythmic segmentation continues during sleep, but may be inhibited by excitement. These move-

ments cause a churning of the contents of the bowel and perhaps to some extent aid peristalsis proper in their onward movement.

Antiperistalsis.—Cannon has found this to be the important motor phenomenon of the large intestine. When the contents of the ileum are emptied into the large intestine they are carried forward for some distance. Antiperistaltic waves then begin and run to the ileocecal valve. A new significance is thus made manifest for the valve. The antiperistaltic waves working toward the closed valve churn the fluid contents and promote absorption. From time to time proper peristaltic contractions move the contents farther toward the rectum.

Periodic movements *en masse* of the colonic contents have been described, apparently distinct from those due to ordinary peristalsis; these movements are more pronounced when the colon is well filled. There are in addition large pendular or swinging movements of the entire colon.

Mechanism of the Movements.—The movements of the bowel are caused by the irritating effect of their contents: solid, liquid, or gaseous. When empty, the intestines always are quiet. The irritation of the contents may be mechanical or chemical. Indifferent substances may act by their temperature or mere bulk. Of gases, hydrogen, oxygen, and nitrogen are indifferent, while carbon dioxide, sulphuretted hydrogen, and the hydrocarbons stimulate peristalsis. Alvarez conceives a progressive gradient of muscular tone, due to variation in muscle metabolism, down the course of the intestinal tract, the maintenance of which is necessary to keep the contents moving in the proper direction.

Englemann believes the stimulus is transmitted through the bowel from muscle cell to muscle cell, but others insist that nervous influences are always necessary. The stimulus to peristalsis originates in the plexus of Auerbach. The plexus of Meissner is concerned with the contractions of the muscularis mucosæ. Bayliss and Starling believe the swaying movements are myogenic in origin. Recent work tends to support the myogenic nature of intestinal contractions.

A progressive difference of electric potential has been found along the course of the bowel from duodenum to colon, orad regions being negative to caudad (Alvarez) and electro-enterographic studies promise to throw further light on intestinal motor function.

A recent study by Carey has demonstrated that the so-called longitudinal and circular musculatures of the small intestine are in reality both arranged in a spiral fashion, the fasciculi of the inner coat forming an almost continuous sheet and making a complete turn every 0.5 to 1 mm. He conceives intestinal action to depend on reciprocal elongating action of the outer and inner coats, superimposed on a tonic condition of equilibrium, and compares the appearance of intestinal movements to those of a left-handed screw.

External Nervous Mechanism.—Stimuli are carried to the intestine through the vagus, and irritation of this nerve causes movements of the whole small intestine and upper half of the large. Irritation of the splanchnic nerves inhibits movements. Cannon, however, has found that section of the splanchnics or of the vagi and splanchnics disturbed

normal peristalsis very little. Other observers, like Bach and Ehrmann, found that the splanchnic nerve is the motor nerve of the longitudinal fibres and the inhibitory nerve of the circular fibres, while the vagus stimulates the circular and inhibits the longitudinal. Bayliss and Starling deny any motor functions to the splanchnic. The lower half of the colon and rectum are innervated through the inferior mesenteric plexus and hypogastric plexus.

Pathological Peristalsis.—Various modifications of peristalsis may be met with. These may consist simply of excessive contractions, but in some cases rolling movements (Nothnagel) cause a contracted loop of the bowel to rotate like a wheel and then relax, while in other cases tonic contractions of a segment of bowel cause a stiffening and narrowing of this portion, which may last some time before it slowly relaxes.

Varieties of Pathological Peristaltic Movements.—(1) Increased peristalsis, (2) tonic contractions; (3) antiperistalsis.

Increased peristalsis may occur: (1) When the bowel contents are abnormal; (2) after the administration of purgatives; (3) after thermic or chemical irritation; (4) after emotional shock; (5) in neurasthenia; (6) from inflammations; (7) in cases of stricture of the bowel.

Tonic Contractions.—When the intestine is empty these convert the tube into a solid cord of a pale color. When a large part of the bowel is affected the abdomen may be scaphoid, as in certain cases of lead colic. Tonic contractions of a loop filled with contents may cause pain. Ordinary and even excessive peristalsis alone does not produce pain.

Pathological antiperistaltic movements are found only in the large intestine, according to Nothnagel. Others, however, believe that such waves may affect the small intestine as well. Greutzer showed that fluid containing free particles introduced into the lower bowel may find its way high up, even to the stomach, in a few hours. This upward movement seemed to occur most actively when the fluid was a sodium chloride solution. It did not occur with potassium chloride or hydrochloric acid solutions. Nothnagel showed that sodium chloride applied to the external wall of the bowel causes upward movements running over several centimeters.

Mucosal Movements.—Animal studies have shown the intestinal mucosa and the villi to have definite, although unrelated, movements, independent of the outer coats of intestinal musculature, but controlled by the muscularis mucosæ. These movements consist of rhythmic contractions of the villi and ridging or grooving of the mucosa. The mucosal motor reaction to stimulation is said to be purely local and myogenic, although the splanchnic nerves and Meissner's plexus ordinarily play a part in its control. This motor activity is said to be most marked in the duodenum and upper jejunum, and it has been suggested that these movements are concerned with the secretion of mucus and the succus entericus, as well as the propulsion of blood and lymph and the mixing of intestinal contents.

Chemical Processes Occurring in the Intestine.—The digestive processes that take place in the intestinal tract are effected by secretions from the glands and lining cells of the intestinal mucous membrane

itself; but, to a still greater extent, by secretions poured into the intestine from the liver and the pancreas. The important secretions are: (1) The pancreatic juice; (2) the bile; (3) the intestinal secretion.

The Pancreatic Juice.—This alkaline liquid is a thin and somewhat watery fluid having a specific gravity of about 1007.5. The amount varies greatly, and cannot be stated with any certainty. In one case in which a permanent fistula existed (Glaessner) the amount was from 500 to 800 cc. per diem; but there is reason to believe that the fluid may not have been a pure pancreatic secretion. The secretion of pancreatic juice begins soon after food has been taken into the stomach, and reaches its maximum during the second to the fourth hour after that time. The character of the food influences, to some extent, the amount of secretion and the time of its maximum flow; and the rate of secretion seems to be especially dependent upon the promptness with which ingested food is discharged from the stomach into the duodenum.

As to the mechanism of pancreatic secretion it was first shown by Dolinsky, in 1895, that acids brought into contact with the mucous membrane of the duodenum promptly excite pancreatic secretion. This effect is certainly to a large extent independent of any influence upon nervous mechanisms, since the result occurs after section of the vagus and splanchnic nerves, quite as readily as when these nerves are intact. More recent work has shown that pancreatic secretion is to some extent under nervous (vagus) control, but that this control is relatively unimportant. Bayliss and Starling demonstrated the probable mode of action. They found in the mucous membrane of the duodenum an enzyme, *prosecretin*, which, under the influence of a 0.4 per cent. solution of hydrochloric acid, is converted into *secretin*. The latter is absorbed and, reaching the pancreas through the blood, stimulates it to activity. It is not improbable that the HCl of the gastric contents may also exercise some effect upon the secretory and nervous mechanisms of the intestinal mucous membrane, but this is not of considerable importance. That secretin is carried to the pancreas in the blood has been proved by the fact that the pancreas may be stimulated by hypodermic injection of secretin.

The ferments of the pancreatic juice are: (1) The proteolytic ferment, trypsin; (2) a diastasic ferment, amylopsin; (3) a lipolytic ferment, lipase or steapsin.

Trypsin.—It has been claimed by some that this is not a single body, but that a variety of trypsins, of different stability, occur. It has also been shown that trypsin is secreted in the form of a pro-enzyme, trypsinogen, which is inoperative as a proteolytic ferment until activated or converted into trypsin by an enzyme derived from the duodenal mucous membrane known as *enterokinase*. Bayliss and Starling claim that the trypsinogen cannot be converted into trypsin except through the action of this duodenal ferment.

Trypsin acts upon proteins in alkaline, slightly acid, or neutral media. Albumins are dissolved by its action without swelling, and, except serum albumin, are converted first into a globulin insoluble in water; later, into peptones soluble in water. Trypsin probably carries the hydrolysis of certain peptones still farther, producing leucin, tyrosin, and other

simple bodies. According to some observations, the prolonged action of trypsin destroys all peptones, leaving only end-products of a simpler nature.

Amylopsin.—This enzyme is similar to, if not identical with, the ptyalin of the saliva. It hydrolyzes starches, with the formation of maltose and achroödextrin. These substances are further acted upon by the maltase of the intestinal secretion, and converted by this into dextrose. According to Hoffmeister, the maximum amylolytic effect occurs in the presence of a moderate acidity.

Lipase or Steapsin.—This ferment was discovered by Bernard in 1849. It has never been isolated. Lipase splits neutral fats, with the formation of fatty acids and glycerin. The fatty acids thus liberated unite with alkalis to form soaps, the latter being further utilized for the emulsification of other fats. By reversed action, lipase causes a synthesis of the products of the splitting of fat, with the re-formation of the original fat. This synthetic action is believed to take place in the intestinal wall, as well as in the tissues. Lipase is a widely distributed enzyme, being found in the blood and in many tissues.

Bile.—The quantity of bile varies considerably under different conditions. The maximum secretion occurs about an hour after a meal. Protein foods increase the amount of secretion; fats reduce it; carbohydrates appear to have little effect. Starling believes that the secretion of bile is initiated by the action of a hormone (analogous with secretin) formed by the action of the acid gastric contents on the mucous membrane in the intestines. The total quantity of bile in twenty-four hours varies from 500 to 600 cc. (Ranke, Wittich, Hammarsten). The bile is a clear, alkaline, mucoid liquid, of yellowish to brownish color. Its important constituents are bile-acid salts (glycocholates and taurocholates) and pigments (bilirubin, biliverdin, etc.). The mucoid character is due to the presence of a nucleo-albumin or true mucin. Various other less important substances are present. There are also ferments, diastasic and lipolytic, which supplement the action of the pancreatic secretion.

The principal action of the bile in digestion and food absorption is its relation to the emulsification of fats. The alkalis contained in the bile unite with the fatty acids to form soaps, and the bile directly aids in the splitting of the fats. It has been held that the bile exercises some antiseptic effect on the intestinal tract; and it probably has some influence in stimulating intestinal peristalsis.

Succus Entericus.—The secretion of the intestinal mucous membrane is the product of various tubular glands of the small intestine. The quantity of the secretion has been estimated (Prigl) as being as much as 3 liters per day, but the amount probably varies widely under different conditions. In the intestinal secretion and in the mucosa of the small intestine there are a number of important enzymes, of which the following have been most thoroughly worked out: enterokinase, erepsin, inverting enzymes, and secretin.

Enterokinase.—This has been found in the mucosa of the duodenum, and seems to be the ferment that actuates trypsinogen, converting it into trypsin. *Secretin* is a stable body existing as a prosecretin in the

intestinal mucous membrane. Under the influence of the acids of the gastric contents the latter is converted into secretin, which is absorbed, and reaches the pancreas through the circulation, stimulating this organ to activity. *Erepsin* completes the hydrolysis of proteins, acting upon the deutero-albumoses and peptones prepared by the preliminary stages of digestion. *Inverting enzymes* convert disaccharids into monosaccharids.

Besides these substances, a secretin has been thought to exist which originates in the intestinal mucous membrane and, after absorption, stimulates the liver to activity.

ABSORPTION OF FOODS IN THE INTESTINE

The products of digestion are mainly absorbed by the bloodvessels, and, entering the portal system, are carried to the liver. Fats, however, after their cleavage in the intestines, are resynthesized in the intestinal mucous membrane and absorbed through the lacteals. *Carbohydrates* are usually absorbed as sugars, monosaccharids, the disaccharids being converted into the simpler form by the action of inverting enzymes in the small intestine. When an excess of sugar is administered there may be direct absorption without such preliminary change. *Fats* are in part split into their constituents, fatty acids and glycerin, and in part emulsified, after which absorption through the mucous membrane occurs. The cleavage products are synthesized and, with the emulsified fat, enter the lacteals. Proteins are absorbed after digestion by pepsin, trypsin, and erepsin, chiefly as amino-acids. These simpler bodies are later synthesized to construct the tissue proteins. It has been claimed that proteins may be absorbed without preliminary digestive alteration.

To some extent, products of digestion that have escaped absorption in the small bowel are absorbed in the large intestine. Under normal conditions the main absorption that occurs in this part of the intestinal tract is that of water; and, as a consequence, the fluid contents of the upper part of the large intestine become more and more concentrated and finally solidified as they approach the rectum.

THE INTESTINES AS EXCRETORY ORGANS

The importance of the intestines as excretory organs is not perhaps as yet fully recognized. It is well known that in certain diseases large quantities of serum may be poured into the bowel, carrying toxic matters of various sorts, chemical, bacterial, etc., and it is probable that a certain proportion of the circulating leukocytes are regularly extruded through the mucosa. Certain inflammatory, ulcerative, and necrotic processes in the mucosa doubtless result from abnormal excretions. Investigations with certain drugs and chemical bodies of other sorts have given direct proof of this excretory function of the intestines. Among other substances, iron, lead, mercury, calcium, strontium and lithium, have been found to be largely excreted through this channel.

AUTOMATIC MECHANISM IN INTESTINAL PROCESSES

The entrance of chyme into the bowel and the secretion of various digestive fluids is regulated in an automatic manner. When the gastric contents reach a certain degree of acidity from the presence of free hydrochloric acid a stimulus is exercised which occasions the opening of the pylorus and the expulsion of the acid chyme. This next acts upon the intestinal mucous membrane, and occasions a stimulus which effects the closing of the pylorus. At the same time, the acid acting upon the mucosa of the duodenum liberates secretin and possibly a hormone which stimulates the liver. To a minor degree, perhaps, the acid excites nervous stimuli, which aid in promoting pancreatic and hepatic activity. The alkaline bile and pancreatic juice entering the duodenum reduce the acidity of the chyme, neutralize it, and render it alkaline, thus establishing conditions favorable for the action of the various ferments. When the acidity of the duodenal contents has been neutralized, the stimulus which caused the closing of the pylorus is removed and a reopening of the pylorus with discharge of more chyme follows. More recently the importance of the acidity of the chyme in controlling pyloric action has been lessened by the discovery that there is a definite reciprocal relation between peristaltic waves traveling along the stomach walls, tonus changes in the stomach, and relaxation of the pyloric sphincter. This relationship is probably supplementary to the acid control of the pylorus.

The inert trypsinogen of the pancreatic juice is converted into trypsin by the ferment enterokinase, which like secretin is liberated from the intestinal mucosa under the influence of the acid chyme. The other ferments derived from the intestinal mucosa are quite possibly secreted as a result of the same cause.

THE FECES

The feces consist of undigested and indigestible residues of food, together with altered digestive secretions, certain excretions from the intestinal mucosa, and a notable percentage of bacteria. Not less than one-third of the dried substance of the feces consists of bacteria, and in some pathological conditions the amount is even greater than this.

The *quantity* of fecal matter depends upon a variety of conditions. The amount of food, its digestibility, the absorptive power of the intestines, the quantity of bile or pancreatic juice, or of mucus thrown off by the intestinal glands, and the activity of bacterial processes in the bowel all influence the amount. Age, occupation, or habits of life, and functional conditions or diseases influencing the degree of peristalsis also exercise a decided influence. On a mixed diet, 120 to 150 grams, representing from 30 to 37 grams of solid residue, are passed in twenty-four hours. The greater the quantity of indigestible residue, the larger the fecal output. The variation of amount in different individuals is very considerable, as is shown in a table of Harley and Goodbody,[1]

[1] *The Chemical Investigation of Gastric and Intestinal Diseases*, 1906.

who found among 188 cases variations from 30 to 282 grams with a mixed diet. The average was 102.8 grams.

The *color* of the feces is largely dependent on the character of the food. With a mixed diet the color is a light or dark brown, and is largely due to urobilin. Large amounts of meat cause a darker color of the stools, on account of the presence of altered blood pigment, hematin, and sulphide of iron. The greenish color seen when an abundance of green vegetables is eaten is due to chlorophyl. The feces passed by persons whose diet consists largely of milk are light yellow, the light color being caused by the quantity of fat in the excreta. Bright-green stools in children or adults may be due to bacterial pigments or to the passage of unaltered bile. Sometimes there is a light color resulting from the presence of bubbles of gas mixed with the fecal matter. The light color of feces in certain liver diseases is due to absence of bile and its derivatives. (See Acholic Stools.) Some medicines, especially iron, bismuth, lead, and silver, cause black stools; while others, like senna, rhubarb, and hematoxylin, cause a yellowish or reddish color.

The *odor* is due to skatol and volatile fatty acids. In fermentative and putrefactive conditions various aromatic bodies may impart a sour to putrid odor. Sometimes all trace of odor is wanting.

The *consistency* is normally dependent upon the amount of water, fat, and mucus associated with the insoluble residues. Lack of digestion and absorption of fat or excess of fat in the diet, excessive water drinking, abnormal excretion of mucus from the intestinal mucosa, and increased peristalsis, all tend to make the stools soft, semiliquid, or even watery. In certain pathological conditions (choleraic diarrhœas) there is an abundant watery outpouring into the bowel, and large watery evacuations result. The stools are more firm than normal when the food contains but little indigestible residue or when in the various forms of constipation the contents are retained too long in the large intestine.

The *reaction* of the normal stool is usually alkaline or neutral. Sometimes, however, a faint acid reaction is met with. Diet and pathological conditions of the bowel may occasion more decided acidity.

The *chemical composition* of the feces varies widely. The amount of water in the feces of persons on a milk diet was found to vary from 73.29 to 79.32 per cent., and in persons on a mixed diet was on the average 75.72 per cent. (Harley and Goodbody). Of the organic substances met with normally, fats and their derivatives, soaps, albumin, mucin, phenol, indol, skatol, fatty acids and their salts are important. The daily excretion of nitrogen in fasting persons has been found to vary from 0.17 gram to 0.446 gram per day, the average being 0.254 gram (Schmidt and Strasburger). With a mixed diet Harley and Goodbody found a discharge of from 0.30 to 1.55 grams per day, the average being 0.97 gram. Excess of diet, especially such as contains a large amount of residue, causes progressive increase in elimination of nitrogen. The percentage absorption of nitrogen of the food, with various forms of diet, varies from 90 to 96 per cent. Approximately, one-half of the nitrogen of the feces is contained in the bodies of the bacteria. Fat, like nitrogenous substances, is excreted in the feces even when the patient is fasting.

The total excretion per day under these circumstances is from 0.57 to 1.21 grams (Schmidt and Strasburger). With ordinary diet, either milk or mixed, the daily excretion is from 3 to 7 grams, the proportion of absorption varying from 91 to 98 per cent. The character of the fats ingested, and especially the melting point, determines to some extent the degree of absorbability. Phenol, skatol, and indol are products of bacterial processes, and their amount is to a large degree dependent on the activity of such processes.

Among the *inorganic* constituents are chlorides and carbonates of alkalis, phosphates of the alkaline earths, and other inorganic salts in small amounts. The amount and source of the calcium salts have excited special interest. It is generally believed that calcium is to an extent eliminated by the large intestine, although some deny this.

Microscopic examination shows undigested particles of food, such as meat fibres, connective tissue, and starch bodies. In inflammatory conditions mucus, pus cells, epithelium, and blood corpuscles may be found, and occasionally portions of exfoliated mucous membrane or portions of tumors of the bowel may be recognized.

Mucus may be found as gelatinous or shred-like particles or as considerable masses, visible to the naked eye, or as stringy formations visible under low powers of the microscope. Mucus from the upper bowel is often colored yellow by bile pigments; that from the colon or rectum is grayish or white. Certain small masses of gelatinous material that resemble mucus on superficial examination, presenting a yellowish color, may prove to be albuminous substances, and small globular masses, like frog spawn, are derivatives of vegetable matter of the diet. Among the crystals in normal feces triple phosphates are the most common. Crystals of neutral phosphate of lime, and of oxalate of lime, cholesterin and Charcot-Leyden crystals, may also be found.

Acholic, Colorless, and Fatty Stools.—*Acholic stools* are yellowish gray or actually white in color. To a large extent this is due to the absence of hydrobilirubin, the normal pigment which is a derivative of bile pigment. In any condition in which complete obstruction of the hepatic or common bile duct occurs the feces become of the color described. Sometimes the same stool occurs without jaundice and without obstruction of the bile duct. In these cases the light color is usually due to the presence of enormous quantities of fat which may be dependent upon disease of the pancreas, obstruction of the pancreatic duct, or to various diseases of the intestines which interfere with the absorption of fat. Chemical analyses have shown in these cases that urobilin is present, although its color is obscured by the excess of fat. Another explanation of colorless stools in the absence of diminished outflow of bile is that the bile pigments are converted into colorless substances (leuko-urobilin). In these cases the stools give reactions for bile, and may be devoid of an excess of fat.

Colorless stools may occur independently of any disease of the liver or pancreas. In various forms of intense diarrhœa, as in dysentery, or certain cases of enteritis, in tuberculous peritonitis in children (Berggrün and Katz), and occasionally in various other diseases, the feces may be

quite colorless. A diminished excretion of bile may play some part in these conditions, but in most cases the altered color is the result of the amount of unabsorbed fat.

Fatty Stools.—Various conditions may occasion excess of fat in the stools. As a rule, however, the term fatty stools is applied to cases in which masses of fat can be seen in the feces or in which there is a distinctly oily appearance. When somewhat watery, oil may collect on the surface of the liquid. Microscopically, fat crystals in large numbers are discovered. Fatty stools may result from:

1. Increased ingestion of fat, as in persons consuming large quantities of milk, cream, olive or cod-liver oil.

2. When absorption of fat is interfered with (*a*) by diseases of the bowel, such as enteritis, ulceration, etc., or (*b*) by active peristalsis and the prompt evacuation of the upper bowel.

3. When bile is excluded from the bowel by obstructions of the bile duct. The excess of fat associated with acholic stools has been mentioned.

4. When disease of the pancreas or obstruction of its ducts causes deficiency of pancreatic juice. In these conditions the most typical fatty stools are met with. A veritable fatty diarrhœa may occur. The association of obstructive biliary conditions often aids in the production of the fatty stools of pancreatic disease. A difference between the fatty stools of biliary obstruction and of lack of pancreatic secretion has been indicated by Müller. In the former condition a large percentage of the fat present (84.3 per cent.) had suffered cleavage, whereas in cases of lack of pancreatic fluid only 39.8 per cent. had been converted.

Intestinal Sand.—Occasionally gritty, sand-like material is discharged from the intestines. This usually consists of granular particles of grayish or reddish color, and on chemical examination has been found to contain the following constituents: Water, 12.40 parts; organic matter, 26.29; inorganic matter, 61.31. The inorganic constituents consisted of calcium oxide, 54.98 parts; phosphorus pentoxide, 42.35; carbon dioxide, 2.20; and a residue containing traces of magnesium and iron, 0.47. The term intestinal lithiasis has been applied to the condition, in the thought that there is a particular form of catarrh of the intestines with the discharge of calcareous matter comparable to the formation of calculi elsewhere.

Intestinal sand is probably formed in the colon, as it usually contains considerable urobilin and little bile-pigment. It must, therefore, be produced in a part of the intestines in which the conversion of bile-pigment has progressed considerably. The condition with which intestinal sand is most commonly associated is mucous colitis.

A condition (false intestinal sand) that requires differentiation is that in which various residues of vegetable food are passed. These may have a sandy character that suggests true intestinal sand.

BACTERIOLOGY OF THE INTESTINAL TRACT

Enormous numbers of bacteria normally occupy the intestinal tract. A conception of the number may be gained from the knowledge that

Strasburger found that one-third of the weight of the dry residue of the feces consists of the bacterial bodies. In normal adults the weight of the dried bacteria passed in twenty-four hours is as much as 8 grams; while in certain dyspeptic conditions it may reach 14 to 20 grams. When habitual constipation is present the weight falls to 5.5 or as low as 2.6 grams.

Distribution of Bacteria in the Intestines.—There are far more bacteria in the large than in the small bowel. Systematic examinations show a progressive increase in number from the duodenum to the large intestine. The duodenum and jejunum may be entirely free six hours after meals (Cushing and Livingood). Below the jejunum bacteria are probably never absent after birth. The kinds of bacteria as well as the number vary in different parts of the digestive tract. This is doubtless due to changes in the conditions in different situations. The gastric secretion, the bile, and the pancreatic juice have probably only a moderate effect in destroying bacteria. Smith and Tennant claimed that the secretions of the intestinal mucosa have an inhibitory effect on the multiplication of bacteria and others have demonstrated specific bactericidal power in the mucosa of the rabbit's small intestine. The condition of the intestinal contents with reference to the process of digestion and the presence or absence of oxygen are factors that have an influence on the number and kind of organisms present in different localities. Herter showed that the conditions are practically anaërobic below the middle of the small intestine.

The principal factors in controlling the intestinal flora are probably the free HCl of the stomach, intestinal peristalsis, the various digestive secretions, antagonism of the normal flora, the nature and amount of the food, the reaction of intestinal contents and the presence of foci of infection in the mouth and upper air passages. The relative importance of these factors has been the subject of controversy, but the character of the food is of undoubted significance in many cases. The organisms generally found in the duodenum and jejunum are various forms of micrococci and other varieties swallowed with food or saliva. In the lower part of the small intestine are found the obligate intestinal bacteria which belong respectively to the groups *Bacillus lactis aërogenes*, *Bacillus coli*, and *Bacillus bifidus communis*. These forms remain as permanent inhabitants and are not dependent on ingestion with food. Although capable of exercising pathogenic properties under certain circumstances, they are ordinarily so adapted to the organism, and it to them, that their presence is devoid of any pathological effects. Although within the intestinal tract, they are practically outside the body, and whatever products are elaborated by their growth normally have little apparent effect on the system. The most abundant of the three forms named is the colon group. Various pyogenic cocci and the colon bacillus are at times found in considerable numbers in the upper small intestine, but the significance of their presence there is not clear. Organisms of the *Bacillus acidophilus* type are often found in normal individuals.

Among the forms met with in the lower small intestine and in the large bowel are certain anaërobes, notably *Bacillus putrificus* and *Bacillus aërogenes capsulatus;* other organisms found at times include the enterococcus, Gram-negative diplococci, various streptococci, and spore-bearing

aërobes with proteolytic power. Many other organisms have been found in the intestinal tract under seemingly normal conditions.

The meconium before birth is sterile. Very soon after birth microorganisms are swallowed or enter the anus, and a considerable flora is soon present. In nurslings the *Bacillus bifidus* is the most abundant form in the large intestine, the *Bacillus coli* being less numerous. In bottle-fed children the dominant form, as in adults, is *B. coli* (Herter).

The Significance of Bacteria in the Intestinal Tract.—Are bacteria in the intestines to be regarded as a normal condition and necessary to life? Nuttall and Thierfelder kept young guinea-pigs, removed from the maternal uterus by Cæsarean section under aseptic precautions, for some weeks in a sterile condition by feeding sterile food and allowing only sterile air to reach them. The animals gained weight and in every way developed as well as the controls. Opposite conclusions have been arrived at by other investigators, who found that animals did not develop in a normal manner when kept free of bacteria (Schottelius, Madame Metchnikoff, Moro). Pasteur and Nothnagel believed that bacteria are essential to physiological life, and certainly, whether essential or not, they are universally present and exercise a distinct effect on the intra-intestinal processes. The role of bacteria in the conversion of bile pigments into urobilin, the final decomposition of products of protein digestion by bacteria, the possible presence of enterokinase of bacterial origin (Dellezenne, Breton), and other evidences may be recalled.

Under ordinary conditions the bacteria of the feces are practically all dead. Klein estimated that a little over 1 per cent. are living forms, and Strasburger found even a lower proportion. The causes of this practical sterilization of the feces have not yet been determined with certainty. Possibly the changing reactions and other conditions at the different levels of the bowel may play some part, as may also influences exerted by the bowel wall and its secretions. Perhaps products of the bacteria themselves occasion their own destruction.

There is considerable evidence to prove that the normal intestinal flora is useful in protecting the individual against accidental pathogenic invaders. It has often been observed that organisms of a type not indigenous to the intestinal tract are soon destroyed, even when introduced in large numbers. There seems to be little doubt that *Bacillus coli* and *Bacillus bifidus* exercise some inhibitory action on the growth of pathogenic organisms such as the putrefactive anaërobes and various specific pathogenic forms. Conradi and Kurpjuweit attribute this effect to antibacterial substances elaborated by the *Bacillus coli*. They believe, also, that the same substances destroy the organism itself, thus accounting for the nearly sterile condition of the feces. Lactic acid formed in the intestinal tract or swallowed with food may exercise a restraining influence on the growth of pathogenic (putrefactive) organisms. This may explain the controlling influence of a milk diet observed clinically in intestinal putrefaction.

Growth and Virulence of Intestinal Bacteria.—Various digestive disturbances may increase the growth of bacteria by causing large amounts of nutritious material to pass down to the lower bowel. The

intestinal walls are undoubtedly permeable to various organisms under certain abnormal conditions, and it is possible that under ordinary circumstances bacteria, such as the *Bacillus coli*, may pass into the blood or lymph circulation to be stopped by the mesenteric lymph nodes or the liver, or to pass further into various other organs. Organisms have repeatedly been found in the mesenteric nodes, and the liver, and have at times been recovered from the portal blood in apparently normal animals. The formerly prevalent belief in tissue sterility has been seriously shaken. In habitual constipation, when practically all absorbable material is taken up in the small intestine, the number of bacteria in the feces is the lowest found under any conditions. The bacterial output was found to be as low as 2.6 gm. as against as much as 20 gm. in dyspeptic conditions and 8 gm. in normal persons (Strasburger). Excessive feeding acts in the same manner as digestive disturbances, and in part as a result of the dyspeptic conditions caused by it. Catarrhal conditions of the bowel, the result of excessive multiplication of the bacteria or occurring independently, favor further increase of bacterial growth and increased virulence of the organisms. When ulcerations, erosions, or other lesions of the mucous membrane are present, the ordinarily harmless intestinal bacteria may gain access to the tissues and may occasion local or general infections. Sometimes a symbiotic relationship is established between different bacterial forms or between bacteria and protozoa.

Diagnosis of the Types of Intestinal Bacteria.—Systematic culture methods are of course required to determine accurately the kinds of organisms present in the intestinal tract. Such examinations are essential in the diagnosis of certain specific diseases such as cholera and dysentery; and occasionally in typhoid, paratyphoid, and allied infections. In other intestinal disorders simpler methods may serve to identify the prevailing types of invading organisms. The stools of breast-fed infants show a predominance of Gram-positive bacilli, while in bottle-fed children the Gram-negative *Bacillus coli* is conspicuous. In adults the latter type is especially marked, while a diet of milk and carbohydrates occasions the appearance of a small proportion of large-sized Gram-positive bacilli and one of meat in considerable amount that of Gram-positive micrococci.

Bacteriophage.—In 1915 Twort observed the inhibition of growth and partial destruction of a micrococcus growing in agar plates, with the presence of watery-looking areas among the colonies. D'Herelle in 1917 reported a similar phenomenon in colonies of the Shiga dysentery bacillus and, believing it to be due to the activity of an ultra-microscopic organism, named the agent *Bacteriophagum intestinale*. This agent is now generally known as *bacteriophage*. Numerous investigations have shown that it is widely distributed, but its chief source seems to be the intestinal tracts of man and the higher animals. It can be indefinitely propagated by transferring cultures of bacteria in which it is present, but cannot be propagated in the absence of living growing bacteria. It increases progressively with bacterial growth, and seems to be a product of the organisms' growth rather than of their disintegration. The "colonies" of phage appear as clear spots on agar plates with bacterial

growth, or may cause a moth-eaten appearance of the colonies of bacteria (Bull[1]).

The typhoid-dysentery-colon group of organisms appears most susceptible to phage action, but the organisms of diphtheria, plague, hemorrhagic septicemia, and cholera, and the staphylococcus and streptococcus are also more or less sensitive. The agent may remain potent for years when sealed, and resists heat and many antiseptics.

The true nature of bacteriophage is not yet known. D'Herelle thought it to be an enzyme secreted by an ultra-microscopic organism which normally inhabits the intestinal tract of many animals and ordinarily acts upon saprophytes, but may acquire virulence for pathogenic bacteria. Others think it to be a ferment produced by "diseased" bacteria, or a manifestation of a nutritional disorder of bacteria.

Bacteriophage has been used by D'Herelle in the treatment of various infections of the intestinal tract in animals, and in human bacillary dysentery, with striking success, but most attempts by others have not resulted so well. It has also been used to immunize animals against certain infections, but final judgment as to its preventive and therapeutic value must await further developments.

Treatment of Bacterial Invasions of the Intestinal Tract.—The problem of disinfecting the gastro-intestinal tract has occasioned much discussion but remains unsolved. The most important element is the proper regulation of diet and the avoidance of all infection of food. This involves the avoidance of all putrefactive contamination of food by proper care in its preservation and preparation, and the withdrawal of such articles as cheese, uncooked fruit, or milk. The careful cleansing of the mouth is also an important element.

The *quantity* of food is of importance. Excessive eating occasions the passage through the intestinal tract of increased quantities of unabsorbed material and favors bacterial multiplication. A strict regulation and limitation of the diet are, therefore, desirable; and remedies such as hydrochloric acid, pepsin, pancreatin, and the like, which aid digestion, may prove beneficial. Sometimes an exclusive milk diet is useful, particularly when albuminous decomposition or putrefaction is conspicuous. In other cases, a strict limitation of carbohydrate foods is required. No general rule can be laid down as individual cases vary widely.

Intestinal antiseptics of various sorts have been tried; but so far none can be said to have a generally useful effect. Small doses of calomel may be helpful, and other laxatives or purgatives may be temporarily beneficial, by cleansing the intestinal tract. Betanaphthol, ichthyol, resorcin, salol, creosote, etc., have been tried, but appear to exercise little, if any, useful effect. Sometimes these remedies may cause more injury to the mucous membrane than to the bacteria; and increase rather than decrease the number of organisms and the activity of the putrefactive process. Sometimes astringent remedies, such as bismuth and tannin, have a useful effect.

A diet rich in animal protein seems to favor the growth of a proteo-

[1] *Physiological Rev.*, vol. **5**, No. 1, p. 95.

lytic flora, while a carbohydrate diet reduces this type of organism markedly, and causes an increase of the *Bacillus acidophilus* and other aciduric bacteria, whose end-products are in many instances considered less harmful to their host than those of the proteolytic group. Advantage has been taken of this fact in the use of high carbohydrate diets (chiefly lactose and dextrin) together with the administration of living cultures of the *Bacillus acidophilus* (in milk, broth or agar blocks) in the treatment of certain forms of constipation, diarrhœa, and other conditions thought to be due to toxins elaborated in the intestinal tract. Although it seems too early to decide finally as to the value of this form of treatment, encouraging results have been reported. The use of cultures of the *Bacillus bulgaricus* failed to give the results expected.

GASEOUS DISTENTION OF THE INTESTINES

The terms *meteorism* and *tympanites* have been applied to the occurrence of abnormal quantities of gases in the intestines, the former signifying acute, the latter chronic, distentions. Normally there is always a certain amount of gas in the bowels, consisting of the constituents of atmospheric air that has remained unabsorbed after having been swallowed, and other gases derived from the blood or from fermentative processes in the intestines. Among the gases present are oxygen, hydrogen, ammonium, carbon dioxide, methane, and sulphuretted hydrogen. The oxygen is mainly that which gains access to the bowel from atmospheric air swallowed with food. It is, however, readily absorbed, and, consequently, disappears in the small bowel, the large intestine being practically free of it (Herter). Carbon dioxide is largely derived from the blood; and the other gases are mainly derivatives of fermentative processes. The amount of gas normally present is small. Abnormal accumulations may be due to increased swallowing of air, to active gas formation within the bowel, and to interference with absorption or escape of the gas from the intestines.

The formation of abnormal quantities of gas by fermentation is an accompaniment of catarrhal conditions of the bowel and of functional intestinal indigestion. Sometimes such fermentative or putrefactive conditions are excited by indiscretions in diet. With many individuals, milk is a common cause of the condition.

Gaseous distention due to failure of absorption or inadequate discharge of gas from the bowel is common in various intestinal diseases. Such distentions are habitually met with in cases of partial or complete intestinal obstruction. In these cases the interference with the discharge of gas from the bowel is the important factor. In catarrhal inflammation and intense congestion the accumulation of gas is due largely to the failure of absorption. This is strikingly illustrated in cases in which a portion of bowel strangulated by volvulus becomes enormously distended. The gases in such instances are partly due to fermentation within the loop, partly to the liberation of carbon dioxide from the blood and to the stagnation of the circulation preventing reabsorption.

In peritonitis and in certain conditions of nervous or functional

weakness of the intestinal walls, gaseous distention results from the inability of the bowel to remove the accumulations.

In hysterical individuals, and sometimes in persons not manifestly hysterical, extreme distention of the abdomen or localized distention may occur. The name *phantom tumor* has been applied to this condition. In many cases it is paroxysmal and transient, but sometimes it proves quite lasting. Many of the instances, however, of supposed chronic phantom tumor have doubtless been cases of idiopathic dilatation of the colon. The explanation of phantom tumors has occasioned some difficulty. There is, probably in most cases, an actual increase in the amount of gas; but the distention is, in part, more apparent than real, being dependent to some extent upon contractions of the diaphragm and of the abdominal muscles. In other cases, a paresis of the abdominal muscles doubtless plays a part.

Symptoms.—The important symptom of meteorism, or tympanites, is the distention of the abdomen. This is usually uniform; but in some cases it affects limited portions of the bowel, and therefore of the abdomen, more than others. Localized collections of gas are not infrequent in association with organic conditions of the bowel. The degree of distention may vary from slight fulness to enormous enlargement, the amount depending upon the resistance offered by the bowel itself and by the abdominal walls. Subjective symptoms are rarely wanting. In acute cases there is often marked discomfort or severe colicky pain. In the more chronic forms constant slight abdominal distress, accompanied from time to time by exacerbations of distention, is complained of. Loss of appetite, coated tongue, nausea, and a tendency to vomiting after slight indiscretion in diet, and other evidences of disordered digestion are frequent. General symptoms, such as drowsiness, listlessness, and a variety of nervous manifestations, including headaches, neuralgias, and even pronounced neurasthenic symptoms, are common.

On physical examination, the abdomen presents a certain type of elastic resistance that is usually quite characteristic; and on percussion the deep note of tympany is more or less pathognomonic. The liver and spleen may be displaced, and their normal areas of dulness obscured or almost obliterated. This is particularly important in the case of the liver, on account of the possibility of mistaking tympany for the accumulation of gas in the peritoneal cavity. In extreme cases the diaphragm is forced upward, and the heart may be displaced, sometimes to the extent of two or three intercostal spaces, and the bases of the lungs may be somewhat compressed. In these instances signs of pulmonary and circulatory embarrassment are usually present.

In cases of phantom tumor symptoms may be wanting, or the patient may complain of various subjective manifestations. A local gaseous distention may simulate an actual abdominal tumor. When the distention is extreme and the normal tympanitic note gives place to a duller tone on percussion, the simulation may be quite confusing.

Diagnosis.—This rarely occasions difficulty. The important question is to determine the cause, and this requires a careful consideration of the conditions in which such distention may occur.

Treatment.—In moderate cases due to irritative and fermentative conditions in the bowel, restriction and regulation of the diet may speedily relieve the condition. Remedies may, however, be required to reduce the distention more speedily. Various carminatives, such as oil of peppermint, menthol, chloroform, Hoffmann's anodyne, asafetida, and the like, are employed for this purpose.

Sometimes the use of laxatives or purgatives may be beneficial, but usually evacuation of the bowels is best accomplished by the employment of enemata containing asafœtida or turpentine in saline solutions, soapsuds, etc. When the distention is excessive, a rectal tube may be useful or suppositories containing asafœtida may be of use. The peristalsis in causing a rapid discharge of gas. Turpentine stupes, flaxseed poultices, may be stimulated by the use of eserine or pituitrin. Hypodermic injections of the sulphate of eserine, in doses of gr. $\frac{1}{100}$ to $\frac{1}{50}$, repeated at intervals of three or four hours, sometimes act satisfactorily.

Puncture of the distended bowel is a dangerous mode of treatment and cannot be advised.

INTESTINAL INDIGESTION

This term is preferable to the name intestinal dyspepsia, sometimes applied to it, because the latter suggests the gastric digestion rather than that of the intestines. In a broad sense, *intestinal indigestion* may be used as a term denoting any form of interference with the normal intestinal functions, but it is more properly restricted to functional derangements, rather than to such as may attend organic disease. In inflammatory conditions of the intestines, in obstruction, in cases of ulceration, tumors, and the like, the normal digestive processes and absorption are interfered with; but these are direct consequences of organic troubles. There remains a group of conditions in which, without gross organic disease, disturbance of the intestinal functions is met with.

Etiology.—Functional intestinal indigestion may be due to (1) lack of bile and pancreatic juice; (2) lack of secretion of the intestinal ferments proper; (3) bacterial fermentative processes.

Attention is directed to the effects of the withdrawal of biliary and pancreatic secretion in the discussion of fatty stools, acholic stools, and diarrhœa. Usually, in the consideration of intestinal indigestion, these conditions are not taken into account. Unfortunately, very little can be said regarding the functional results of insufficient secretion of intestinal ferments proper. That these secretions play an important rôle is entirely probable but the clinical significance of derangement of these secretions has not been determined with any definiteness.

Disturbance of the intestinal digestion may be a *secondary* result of the disorders of gastric digestion. In cases of hyperacidity of the gastric contents the alkalinity of the bile and pancreatic juice may be insufficient to neutralize the acidity of the chyme, in consequence of which the reaction of the contents of the duodenum and jejunum remains acid, instead of being alkaline. This interferes with the normal pancreatic digestion, and at the same time subjects the mucosa of the upper small

intestine to irritation. A similar effect may follow insufficient secretion of bile and pancreatic juice, in which case the normal acid chyme may fail of neutralization. Much more common is the development of acidity in the small intestine as the result of bacterial invasion. This is very common in infants and children. Bacterial decomposition of milk and other foods may occasion the formation of lactic, acetic, and other acids, and may thus interfere with pancreatic digestion and irritate the mucosa of the small bowel. The effects of these conditions are, first, an interference with normal intestinal digestion; second, an increased liability to bacterial activity; and, third, irritation of the mucosa.

Symptoms.—These are partly gastric and partly intestinal. Among the gastric manifestations, nausea, vomiting, flatulence, and sensory disturbances, such as heaviness or pain, may be mentioned. Among intestinal manifestations are gaseous distention and diarrhœa. The acid contents provoke an irritation of the upper bowel and the formation of the excessive quantities of mucus. At the same time, peristalsis is increased by the irritation; and the semifluid contents of the upper bowel are hurried into the lower bowel and discharged before normal inspissation and chemical changes have time to occur. The stools are acid instead of alkaline, and frequently cause marked irritation of the rectum and anus. In children this is an important symptom; and intense irritation may be met with. The movements are usually somewhat tenacious, on account of the admixture of excessive quantities of mucus, and commonly present a greenish color, on account of the presence of bacterial pigments or of unaltered bile. In a special form described by Schmidt, under the name of *intestinal fermentative dyspepsia*, the stools are of light color, foamy, and of a musty or sour odor, due to the presence of butyric acid. When functional indigestion persists, the irritation of the bowel readily passes into catarrhal inflammation.

Diagnosis.—This often presents great difficulty. In some instances the symptoms are vague and indistinct; and it may be difficult to determine that a continuous tendency to intestinal flatulence and slight disorder of the bowel is due to functional disturbance rather than to organic disease. In more acute cases, especially in children, the evidence is more trustworthy. The occurrence of mucous, gelatinous stools of green color, acid reaction, and sour or musty odor, is strongly significant of this form of disease. It is always difficult, however, to determine that an actual catarrhal enteritis has not supervened.

Treatment.—This requires close supervision of the diet. In the beginning of acute attacks, the withdrawal of all food may be advisable. In children, as well as in adults, the substitution of albumin water, broths, soups, or barley water for the ordinary diet, and especially for a milk diet, is advisable. Later, the food should be regulated according to the nature of the case. Sometimes, when fermentative processes and gas-formation are conspicuous, it is best to use only animal food, such as eggs, soups, jellies, and gelatin preparations; while in other cases, in which albumin decomposition predominates, gruels, cereals, and farinaceous foods generally, with smaller amounts of albuminous food, should be given. In the latter type of case the administration of

living cultures of the *Bacillus acidophilus* in milk (500 to 1200 cc. daily), broth, or agar cultures may prove of assistance in controlling the tendency to excessive protein decomposition.

The medical treatment is directed to the evacuation of the contents of the intestines and the removal of fermenting material. A full dose of castor oil, or repeated small doses, may accomplish this purpose. Calomel in small amounts (gr. $\frac{1}{40}$ to gr. $\frac{1}{10}$), two or three times daily, may exercise an antiseptic effect, as well as a slightly laxative influence. Other remedies like salol, betanaphthol and guaiacol carbonate may be tried. After the upper bowel is free of fermenting contents, bismuth, chalk mixture, or other mild astringents may be desirable to allay irritation and check further diarrhœa. Pancreon, prepared by treating pancreatin with tannin, is recommended when intestinal indigestion is due to decreased secretion of pancreatic juice. It is administered in water before meals in a dose of gr. vj (gm. 0.4). In cases in which gastric disorders have preceded the intestinal disturbance the treatment should be directed primarily to the condition of the stomach.

INTESTINAL COLIC

Definition.—The term intestinal colic should be restricted to attacks of paroxysmal intestinal pain caused by violent tonic contractions of the bowel resulting from undue stimulation of the intestinal nerves or from obstructive conditions. The more or less continuous pain and tenderness of inflammation of the bowels or peritoneum, and the purely neuralgic pain (*enteralgia*, in the strict sense) should not be included.

Etiology.—The immediate cause of the pain of colic is the excitation of the intestinal nerves and the violent tonic contraction of the bowels caused by irritating intestinal contents or by obstructive conditions. The cases may be divided into those in which there is mainly functional disturbance and those associated with organic conditions.

Colic Due to Functional Disturbances.—Some persons are so sensitive that even when the food or other ingesta are wholesome, slight causes such as exposure to cold, fatigue, anger, fright, or other emotional conditions, occasion attacks of colic. It is probable that under these circumstances digestion and absorption of food products are interfered with, fermentation or putrefaction occurs, and irritation of the intestinal nervous mechanism takes place. More commonly, colic results from a definite error in diet. The eating of coarse foods, unripe fruit, indigestible substances of all sorts, especially if in excessive quantity, is perhaps the commonest cause. The drinking of cold water, beer, or other liquids at the same time may add to the disturbance, or may alone suffice to bring on an attack. Developmental conditions causing functional weakness or chronic conditions of the bowel, such as partial stenosis, may predispose to attacks of colic under relatively slight provocation, such as overeating. In infants or young children the connection between dietetic errors and colic is nearly always apparent. Frequently such coöperating causes as exposure to cold, fatigue, or emotional disturbances may play an important etiological part. Idiosyncrasy also contributes,

some persons finding it impossible to eat certain, usually wholesome, articles of food without suffering an attack. Whether the ingested food is inherently irritating or is rendered so by the condition of the patient at the time, or his idiosyncrasies, the result is a violent irritation of the nerves of the intestines and a forcible contraction of the muscles of the intestines which causes the painful paroxysms. If the amount of food residue and gaseous accumulations in the intestinal canal is excessive, the obstacle thereby offered to the contractions of the bowel becomes an added cause of pain. Nearly always some sort of obstacle to the free movement of intestinal contents is more or less responsible for attacks of colic. In some cases violent irritation of highly noxious substances may occasion a spasm or paresis of a segment of bowel which thus becomes practically a seat of obstruction. Mere distention of the bowel by gases does not occasion colicky pain, as may be seen in the comparative freedom from all pain in cases of quite marked meteorism and the different type of discomfort or pain in excessive distention.

Certain special substances may act in a direct way upon the nervous mechanism of the bowel. This is seen in the intense colic of lead poisoning and the colicky pains caused by certain laxative medicines.

Fecal accumulations may cause purely functional colic, although they are usually associated with some organic condition. When a considerable impaction has occurred, the peristaltic efforts of the bowel above the accumulation become more and more severe until finally tonic contraction ensues and an attack of colic results.

Colic Due to Organic Conditions.—Foods may prove so irritating to the bowel that an actual catarrhal inflammation is occasioned. This happens quite frequently in children when tainted milk is taken and in adults when bacterial decomposition causes putrefactive changes. The catarrhal inflammation adds to the irritability of the intestinal nerves and increases the tendency to an attack of colic. Ulceration of various sorts of the large or small intestine, such as tuberculous, typhoidal, stercoral, or simple follicular, may occasion genuine attacks of colic. The association of colic with appendicitis is exceedingly common, and may be due to violent contractions of the appendix itself (appendicular colic) or the ileum or colon. All these inflammatory lesions may excite tonic peristaltic contractions, and the partial obstruction increases the obstacle to the movement of the intestinal contents from above.

Symptoms.—The ordinary attack of intestinal colic due to functional disorder of the bowels is usually sudden in onset, beginning with violent cramp-like pains in the umbilical region which spread in various directions. As the peristaltic movements advance from one part to another the patient experiences a change in the position of the pain, and there may be at the same time a sense of movement of gases from one coil of intestines to another. In very severe attacks the pain is more fixed and cannot be definitely localized. The patient at first moves from side to side, draws up his leg, and presses his hands or a pillow against the abdomen, and finally assumes a constant position with thighs flexed toward the abdomen. Pressure usually affords relief, but if inflammatory conditions of the bowel are present, pressure may increase the pain.

In young children an attack of colic is indicated by crying, restlessness, drawing up of the legs, violent contractions of the facial muscles, and later by abdominal distention. Rumbling sounds or borborygmi may indicate the movement of gases in the bowels. Usually attacks of colic subside after a duration of from a few minutes to some hours, and when gas has been discharged or the bowels evacuated. In severe cases the attacks may continue unabated for several or many hours and the patient may grow faint or suffer partial collapse, breaking out into a cold sweat and growing quiet from exhaustion. Severe attacks may also be attended with nausea and vomiting. The temperature is usually little altered, but a moderate degree of fever is not uncommon.

After relief from the primary attack, exacerbations and remissions may follow until the bowels have been thoroughly evacuated or the irritation otherwise removed. A certain amount of abdominal soreness and tenderness may remain after the attacks have ceased and a return to normal intestinal conditions may require several days.

The bowels at the onset of colic are usually constipated. When relief begins there is usually some discharge of flatus and evacuation of the lower bowel; later, a diarrhœal condition may follow, particularly if catarrhal inflammation has accompanied the attack or occasioned it.

Attacks of colic in which the irritation has been sufficient to cause an inflammatory condition are more severe and lasting than those in which the derangement is only functional. Disturbances of the stomach, abdominal distention, soreness and fever are also more likely to occur in these cases; and after relief from the acute condition tenderness and pain, dirrahœa, and sensitiveness are apt to persist for some time.

Colic, associated with organic diseases of the bowels, such as intestinal obstruction from carcinoma, bands, internal hernia, fecal impaction, etc., will be considered in the discussion of those conditions.

Enteralgia or *neuralgia of the intestines* in the strict sense is a rare condition, and to be distinguished from colic by reason of the fact that it is probably not dependent on a tonic intestinal contraction, but rather on a direct painful irritation of the intestinal nerves. Such a condition occurs in hysterical persons and in association with tabes and other organic spinal diseases. The attacks are sudden and severely painful, but unattended with the usual indications of colic. There is intense sensitiveness on pressure, and relief occurs independently of evacuation of the bowels. The general appearance of the patient suggesting a neurotic origin of the pain is more or less characteristic.

Diagnosis.—It is often exceedingly difficult to determine the nature of an attack of abdominal pain having the general features of intestinal colic. The serious character of other conditions which simulate its features requires that these be carefully considered before an attack is regarded as simply intestinal colic. Among other conditions, biliary, renal, and uterine colic must be thought of; the similarity in the symptomatology of rupture of a gastric or duodenal ulcer must be remembered; and above all else, on account of its frequency and seriousness, *appendicitis* must be kept in mind. The last-named offers the greatest difficulty; but if local pain, tenderness and rigidity, fever, leukocytosis,

marked gastric symptoms, obstinate constipation, disturbances of the pulse, and the general condition of the patient be carefully considered, a mistake in diagnosis is not likely to be frequent.

Certain less frequent conditions may require consideration. Among these, acute pancreatitis, the passage of a pancreatic calculus, embolism or thrombosis of the mesenteric vessels, and referred pains, such as those occasionally experienced in the abdomen in cases of thoracic diseases, as pneumonia, pleurisy or angina pectoris, or in pelvic diseases, must be remembered. Occasionally intense epigastric or umbilical pain, associated with nausea and vomiting, is seen at the onset of diabetic acidosis. The onset of acute intestinal obstruction must be carefully distinguished. Usually the failure to relieve the attack by simple measures establishes the diagnosis. In cases of chronic intestinal obstruction the significance of attacks of colic may be overlooked. A partial obstruction may be unattended with marked symptoms until an attack of acute colic occurs. The possible association of this with a chronic condition must be remembered.

Treatment.—Intestinal colic readily subsides when the bowels are evacuated and the local irritation is controlled by various warm applications and by the use of sedatives. If the diagnosis is assured, the bowels may be emptied by the use of a large injection of warm water or soapsuds, to which castor oil or sweet oil may be added; or by the administration of a dose of castor oil if the stomach permits. Salines, calomel, or other purges may be used if the urgency of symptoms does not require speedier agents.

Small doses of opium or morphine not only allay pain but relax spasm, and thus sometimes aid in securing purgation. Various carminatives, such as spirit of chloroform, oil of peppermint, menthol, or camphor water may be combined with opiates, especially when gaseous fermentation is present. A prompt hypodermic injection of morphine, followed by measures to relieve the bowels, may cut short an attack of threatening severity. Local measures, such as hot-water bags, hot fomentations, poultices, etc., give relief, and by relaxing spasm may secure evacuation of the bowels.

In children, hot applications applied locally, hot baths, carminatives with paregoric, mild laxatives, such as castor oil with paregoric, magnesia, calomel, and enemata suffice for severe attacks, while the milder paroxysms are relieved by using soda-mint, oil of peppermint, aromatic spirit of ammonia, or Hoffmann's anodyne.

Lead Colic. A peculiar form of colic occurs in subacute lead poisoning, and is commonly known as lead colic, painter's colic, etc. The important symptom is intense cramp-like pain attended with obstinate constipation. The abdominal muscles are found rigid and contracted, so that the abdomen is flat or even hollow. Other indications of lead poisoning are commonly present, and a blue line along the edges of the gums where they join the teeth is almost pathognomonic. It should be remembered that not infrequently a moderate leukocytosis is present.

Treatment. -This is directed to the relief of the symptoms and the elimination of lead from the system. In the early stages magnesium

sulphate should be given freely to convert any soluble lead salts in the stomach or bowels into the insoluble sulphate and to relieve constipation. At the same time opium may be given by the mouth or rectum, or hypodermics of morphine may be used to allay pain and relieve the intestinal spasm. Free venesection gives prompt relief in some cases. Recently it has been reported (Aub, Fairhall, *et al.*) that calcium metabolism is directly related to the excretion of lead, and good results have been obtained from the administration of calcium during acute symptoms of plumbism, with resultant lessened excretion of lead. After subsidence of the acute symptoms, a low-calcium diet, with phosphoric acid (20 cc. of the dilute acid in water every hour for 10 doses, daily for a period of two weeks) or ammonium chloride (1 gm., 10 to 12 times daily) is recommended. If these drugs are used the appearance of acidosis should be carefully watched for.

INTESTINAL HEMORRHAGE

Etiology.—The causes of hemorrhage from the bowel are exceedingly numerous. In some cases it occurs without any definite organic lesion; but more commonly, hemorrhage signifies some definite change.

Hemorrhage Unassociated with Pathological Conditions of the Bowel.—In association with certain hemorrhagic diatheses or diseases, such as purpura and scurvy, and in some infections, such as septicopyemia and yellow fever, hemorrhage may occur without preceding alteration in the mucous membrane of the bowel. At the time of the hemorrhage, or before it sets in, extravasation of blood into the mucosa may occur; and the source of the hemorrhage may be such an area. Occasionally hemorrhages occur from the mucous membrane of the bowel without any discoverable lesion. Such cases have been met with in tuberculous individuals. It has been claimed that hemorrhages of this sort may take place as a vicarious manifestation of menstruation.

Hemorrhage as the Result of Congestive Conditions of the Bowel.—In cases of cirrhosis of the liver, valvular disease of the heart, and hemorrhagic infarction of the bowel following embolism or thrombosis of the mesenteric vessels, hemorrhage may result. Similarly, in cases of intussusception, strangulation of the bowel, or hernia, there may be hemorrhage as the result of overdistention of the bloodvessels.

Hemorrhage as the Result of Diseases of the Bloodvessels.—The most frequent cause of hemorrhage from the bowels is hemorrhoids. Other diseased conditions of the bloodvessels may, however, occasion hemorrhage. Thus in aneurism of the hepatic artery, rupture may take place into the bile passages, and discharge of blood from the bowel may ensue. Similar conditions of the intestinal vessels occur more rarely. Amyloid degeneration of the intestinal vessels is a common cause of extravasation into the bowel. In grave anemias and in severe infections, degeneration and rupture of the bloodvessels may be the cause of enterorrhagia. Sometimes in chronic nephritis considerable intestinal hemorrhage may occur, probably resulting from degeneration of the bloodvessels and increase of arterial tension.

Hemorrhage as the Result of Inflammatory and Ulcerative Conditions.—In cases of gastric and duodenal ulceration and in typhoid fever hemorrhage occurs frequently. Less marked hemorrhage often attends carcinomatous ulceration; while in ulcers of other sorts, loss of blood although less marked, may be met with. In inflammatory affections of the bowel without ulceration, hemorrhage is much less common. If the inflammation is intense and the congestion is marked, some loss of blood may occur, although free hemorrhage is unusual. Continued slight bleeding is caused by certain parasites, notably hook-worms.

Symptoms.—Ordinarily, no difficulty occurs in the recognition of hemorrhage from the bowels, but it may be difficult to determine the source. As a rule, when the blood comes from the colon or rectum its color is a bright red, and on microscopic examination the corpuscles are well preserved. When hemorrhage occurs from the upper bowel, unless active peristalsis causes its rapid discharge, secondary changes are usually observed. The stools become dark and often tarry in appearance, and are usually highly offensive from decomposition. In many cases there may be a gradual loss of blood from the bowel of so slight a degree that a naked-eye inspection of the stools does not reveal any evidence of hemorrhage. In such cases an examination for occult blood may show its presence. In cases of larger hemorrhage a microscopic examination may discover crystals of blood-coloring matter and dark amorphous pigment. In cases in which inflammatory lesions, ulceration, and especially carcinoma, have occasioned hemorrhage from the bowels, the blood is often associated with mucus and pus, as well as with epithelial cells and other tissue elements.

Hemorrhage from the bowels rarely occasions pain. If the loss of blood is great, the symptoms are those of extensive hemorrhage from any source. After a hemorrhage, intestinal symptoms often develop as the result of putrefactive changes in the blood retained in the intestinal tract. Secondary diarrhœa may be set up as a consequence. Repeated small hemorrhages from the bowel may occasion extreme anemia.

Prognosis.—The result of intestinal hemorrhage depends entirely upon its cause. Severe losses of blood are in all cases serious; but sometimes very extensive hemorrhages are followed by no material impairment of health. In cases of hemorrhoids, as well as in cirrhosis of the liver or other obstructions of the portal circulation, actual improvement may be observed. Repeated losses of blood are of more moment; and when intense anemia has developed, the prognosis is always grave

Treatment.—This must always depend upon the cause, although certain general rules may be formulated. Local applications of cold, such as the ice-bag, are commonly employed, although their value is doubtful. Injections of ice-water into the rectum and colon may, perhaps, be valuable in some cases of hemorrhage from these parts, but in other instances may be actually harmful, by stimulating peristalsis.

Colonic douches may be beneficial when the source of the hemorrhage can be reached in this way. Solutions of nitrate of silver, tannic acid, or other astringents, may be employed. If the hemorrhage cannot be reached, such injections, however, may be objectionable; because, by irritation, they may stimulate active peristalsis and renewed hemorrhage.

Opium has been universally employed for its effect in controlling peristalsis and quieting the patient. The judicious use of this drug is advisable in some forms of intestinal hemorrhage; but it should not be used to such an extent that the bowels are completely locked and the blood and other materials therefore retained and permitted to undergo putrefactive decomposition. Astringent remedies, such as nitrate of silver, acetate of lead, bismuth salts, and tannic acid preparations, are sometimes useful. The calcium salts may be given. Ergot, hydrastis, and turpentine are of doubtful value. Horse serum, whole human blood, or various tissue coagulants may be injected intramuscularly. Certain cases, with grave anemia or shock, may demand the transfusion of blood from a suitably matched donor.

CONSTIPATION

Synonyms.—Habitual constipation; obstipation.

Definition.—Infrequency in the evacuation of the bowels and a tendency to abnormal dryness or hardness and reduction in the quantity of the feces are the conditions comprised in the term constipation. It is difficult to give a positive definition, since the physiological limitations vary widely. In most healthy persons there is normally an action of the bowels once in twenty-four hours, and when the conditions of life are uniform this occurs at approximately the same time of day. When the intervals are two or three days, even though symptoms are absent, the condition must be regarded as one of constipation. Instances have been reported in which there was but one movement in two or three weeks, the patients presenting no symptoms of disease. Such must be regarded as cases of decided constipation. Sometimes, although the movements occur daily, the quantity is decidedly below normal and the character of the movements inspissated. In other cases, by testing with charcoal or carmine, it may be found that, although an approximately normal movement is evacuated daily, the duration of time in the intestinal tract has been prolonged. This has been defined as *latent* constipation. Essentially, then, delay in the evacuation of food residues and abnormal inspissation, with a reduction in the quantity of the excreta, constitute the condition under discussion, whether symptoms be present or not.

Some authorities tend to limit the term to purely functional conditions, excluding cases in which organic disease of the bowel is present. This cannot, however, be fully accomplished; for such conditions as ptosis of the colon, movable cecum and redundancy of the sigmoid are often encountered in patients with habitual constipation, and other minor intestinal lesions cannot be excluded, though it is fully understood that constipation resulting from definite intestinal diseases (adhesions, strictures, etc.) is merely a symptomatic result of such disease.

Etiology.—Any discussion of the causes of constipation must be based primarily upon a knowledge of the physiological processes concerned in the onward movement of the intestinal contents. The efficiency of the peristaltic movements will depend upon the normal strength of the muscles of the bowel, the integrity of the nervous mechanism, the

amount of residue in the intestinal contents and its character. Solid contents, water and other liquids, or gases, may serve as stimulants either mechanically or chemically. Sometimes the irritation results from the mere bulk of the contents; more commonly, the mechanical nature determines the effect. Thus, coarse and irritating substances and insoluble residues are particularly exciting. Of gases, hydrogen, oxygen, and nitrogen are said to be indifferent, while carbon dioxide, sulphuretted hydrogen, and volatile hydrocarbons stimulate activity.

The onward movement of the residual matter left in the bowels after complete digestion is the result of the peristaltic movements. Through this agency the contents traverse the small intestine in the course of a few hours and the large intestine in from twenty to twenty-four hours. The slower progress in the colon is probably the result of the frequency of antiperistaltic waves.

The final evacuation of the feces is caused by reflex stimuli produced by irritation in the rectum resulting from the presence of feces and the direct voluntary expulsive efforts which involve contractions of the abdominal muscles. The preservation of a normal rectal reflex is of the greatest importance and its loss or diminution is the important factor in certain cases of constipation.

The condition of the abdominal muscles plays a further part in the whole process of the movement of the intestinal contents in that the condition of these muscles and the effect of their normal contraction influences very largely the activity of the peristaltic contractions of the intestines. The integrity of the abdominal muscles is of course highly important also in the act of defecation.

It will be seen that abnormal sluggishness in the movement of the contents of the bowels may be the result of (1) the character of the food residues; (2) weakness of the intestinal muscles; (3) impairment of the nervous mechanism; (4) weakness of the abdominal walls.

In addition to the causes of reduction in the normal motor function it seems probable that abnormalities in the absorption processes may be of importance. Some authors (Schmidt) insist that there is excessive digestibility of cellulose as a result of which this most important stimulant to peristaltic activity is withdrawn. Others have suggested that rapid absorption of water and premature inspissation of the feces in the upper part of the large intestine is an important factor.

Finally, perverted intestinal contractions causing spasms of localized or considerable portions of the lower bowel or, on the contrary, segments of partial or complete atony, may prevent the onward movement of the fecal matter.

Functional Causes.—There may be considered under this head conditions which produce torpor of the intestines themselves and conditions which cause a weakness of the diaphragm and abdominal walls, and thus lead to reduction in the expulsive power or indirectly to weakening of the intestines themselves. We may also include causes of spasm of the bowel or of abnormal absorption.

Intestinal torpor may occur acutely and as a result of various nervous conditions. Thus, as a result of fear or other emotions and nervous mani-

festations in neurasthenia, melancholia, and the like, intestinal atony and constipation are not infrequent. Frequently this torpor results from habit. The normal individual tends to evacuate the bowel after the first meal of the day, probably for the reason that at this time the food residue of the previous day has reached the lower bowel and that the ingestion of food into the stomach, together with the change of position of a person from the recumbent to the upright, and the exercise taken up with the day's work, excite peristaltic contractions and the tendency to evacuation. When, as a result of lack of time or inattention, this stimulus is ignored or resisted, the desire passes, and with repetition of such neglect the habit of longer retention is established. The normal stimulus from the lower bowel becomes less and less effective, and eventually chronic constipation results. Long retention of fecal matter in the lower bowel causes dilatation of this portion of the bowel and a weakening of its expulsive power. In individuals suffering from long-continued constipation, considerable pouching of the sigmoid, descending colon, and rectum is not infrequent. Certain authors assume that there is some special form of impairment of the innervation of the muscles, especially of the colon and rectum, but fail to make clear the manner of its occurrence. Similarly it may be assumed that in certain persons there is some inherent weakness of the intestinal musculature.

Diseases of the *stomach* frequently occasion chronic constipation. In some instances this may be the result of the long retention of food in the stomach owing to the reduction of its motor power or obstruction of the pylorus, and possibly stimuli normally propagated from the stomach to the intestine fail to be generated. In addition, the contents of the stomach may be transmitted to the intestine in such condition that irritation of the bowel is first produced, and later spasmodic or tonic contractions which cause the resulting constipation.

The *dietetic* causes are numerous and most important. The habitual use of food which leaves little residue is a very frequent cause. The constipating effect of a milk diet is thus explained. Similarly, the use of highly concentrated food, such as meat, eggs, etc., with little addition of vegetables, which contain a relatively large amount of unabsorbable residue, may produce habitual constipation. The neglect of vegetables, besides causing a reduction in the amount of residue, removes from the diet a large proportion of the neutral salts which are normally active in regulating the action of the bowels. Occasionally the bowels become constipated as a result of the eating of foods which contain an excess of irritating residue, such as berries containing small seeds or vegetables rich in cellulose. This form of constipation is due to *spasmodic* conditions of the bowel caused by the irritation. In many persons the cause appears to be insufficient water, and the resulting dryness of the intestinal contents; or the drinking of hard water containing large quantities of lime salts may be at fault.

Bacteria play an important rôle in the normal as well as in the abnormal conditions affecting the intestinal tract. The number of bacteria in the feces of constipated persons is decidedly smaller than in those of normal individuals. This is, in part, due to the fact that the sluggish

peristalsis occasions a longer retention of food in the bowel, and consequently a fuller degree of absorption of the nutritious element. As a result, the bacteria which mainly flourish in the lower intestinal tract are deprived of pabulum and multiply less freely, in consequence of which fatty acids, gases, and other products of bacterial growth are wanting and the stimulus to peristalsis normally exercised by these products is lacking. To some extent the bacteria also excite mucus formation in the normal bowel, and this aids as a lubricant and helps to keep the feces soft.

Congestion and inflammation of the bowels in certain cases cause constipation by directly weakening the contractions, but this mode of causation is probably far less frequent and important in genuine habitual constipation than was at one time assumed. It would appear that chronic constipation is more usually the result of disorder of the nervous mechanism which controls peristalsis than of any direct weakness of the wall of the bowel. It cannot be denied that inflammation or congestion, and especially such conditions as congenital or acquired dilatation of the bowel, may produce constipation by direct weakness of peristalsis, and it is contended only that such factors are of relatively little importance compared with reduced motility through alterations in the contents of the bowel or of the neuro-muscular mechanism.

Various causes operate to produce constipation by causing weakness of the diaphragm or the abdominal walls. A direct effect is probably exerted upon the movements of the intestine by the contractions of the abdominal muscles, and it is probable that a normal condition of tone in the abdominal walls has a certain reflex influence in producing a like state in the underlying organs. Furthermore, relaxation of the walls of the abdominal cavity allows of dilatation of the contained hollow viscera, which interferes with the effectiveness of the contraction of these organs. Various conditions which cause weakness, either of the diaphragmatic movements or of the abdominal parietes, occasion sluggishness of the bowels. Thus in chronic thoracic diseases, such as emphysema, pleural adhesion, etc., more or less obstinate constipation may occur. The effect of weakness of the abdominal walls is evident in the constipation that occurs after repeated pregnancies or when large accumulations of fat have been deposited in the omentum or abdominal walls, or with various abdominal tumors. Constipation may reach high grades in cases of decided separation of the recti as a result not only of the weakness of the superficial structures but also of enteroptosis.

Dress probably has a certain amount of influence as a cause of constipation. The much greater frequency of this disorder in women may be attributed to lack of equal exercise, to the more frequent neglect owing to inconvenience of surroundings, etc., and possibly to certain anatomical considerations; but it is not improbable that the character of clothing has something to do with this greater prevalence in women. The weakness of the abdominal walls which results from constriction of the lower chest and abdomen may be a contributing cause.

Sedentary life and lack of exercise operate in a variety of ways. In the first place, there is a tendency to digestive disturbance and a lack

of general systemic tone, and in a more direct way these conditions may operate by producing weakness of the abdominal muscles. Some individuals normally perfectly regular become constipated when confined to the house by some trivial ailment which merely restricts the usual exercise. The same result also occurs on long railway journeys or sea voyages, and is especially marked in patients confined to bed through some injury or a disease not affecting the abdominal walls directly.

Organic Causes.—More attention was formerly paid to strictly organic conditions in the development of habitual constipation than is now given to such conditions. Undoubtedly adhesions or partial obstructions by stenoses of localized segments of the bowel or constricting bands surrounding a coil of intestine may be the occasion of intense and long-continued constipation. Similarly, uterine displacement, pelvic tumors, malpositions of the intestine (enteroptosis), or congenital or acquired malformations (idiopathic dilatation of the colon) may be of importance in certain instances. Likewise, certain conditions affecting the efficiency of the expulsive efforts, such as a weakened perineum from lacerations, and diseased conditions or relaxation of the abdominal walls, may be of some influence. Failure of the ileocecal valve to function properly, thus allowing cecal contents to return to the ileum, has been considered an important factor in stasis by some. It is difficult to determine how far the term habitual constipation may be extended to include such organic conditions. Those who contend for the limitation of this term to functional conditions do not exclude ptosis of the transverse colon, which in a sense acts as an organic or mechanical cause of delayed peristalsis and of onward movement of the intestinal contents quite as much as adhesions.

Functional Types of Constipation.—Attempts to divide cases of constipation into different types have not been specially satisfactory, but something is gained by recalling such classifications.

(*a*) *Atonic Constipation.*—We may include here various causes such as dietary errors (alimentary constipation), general or local weakness, habits of irregularity of defecation and reduced force of expulsion, etc.

(*b*) *Spastic Constipation.*—As a result of irritable conditions of the bowel itself or reflexly, localized or extensive spasms, sometimes shifting, sometimes more fixed in location, may occur.

Roentgen-ray Findings.—A study of the movement of the intestinal contents in cases of constipation usually shows but little retardation in the small intestine, though its complete emptying may be manifestly delayed. In the large intestine there is a distinct delay which may be most manifest in different localities in different cases. In some the bismuth accumulates in the cecum and very little, if any, reaches the hepatic flexure after eighteen or twenty-four hours; in others, especially when there is decided ptosis of the transverse colon, the most marked delay is seen in this portion; in a third group the delay is most marked in the descending colon or sigmoid flexure. In cases of spastic type affecting the descending colon or sigmoid the skiagram of these portions may plainly indicate the narrowing of the contracted bowel. When constipation is largely the result of retention in the rectum and reduced expulsion enormous enlargement of the rectum may be seen.

Pathology. In a majority of cases but little structural alteration can be detected. Certain resulting conditions are met in a certain number of the cases. Nearly always there is some abnormal distention of the sigmoid and rectum, and when constipation has been extreme and prolonged, distinct pouches or diverticula may be produced. In some instances these contain hardened scybala and inflammatory materials, and ulceration of the mucous membrane may occur (stercoral ulceration). Hardened scybala may produce severe catarrhal inflammation.

Marked distention of the colon, with thinning of the mucous membrane and of all the walls, may result from obstinate constipation, especially when accompanied by frequent impactions in the lower bowel. The small intestine rarely shares in such distentions. More commonly there may be narrowing of the lumen and thickening of the wall in limited segments due to long-continued or repeated spasmodic contractions, especially when habitual insufficiency of food has been a principal cause. The writer has repeatedly met with such contracted areas of the bowel in autopsies in cases of chronic insanity in which there has been long-continued insufficiency of food and resulting constipation.

Sometimes infiltration of the inspissated fecal masses or scybala with salts of lime or magnesium may result in the formation of so-called "coproliths." These are always found in the large intestine.

Symptoms.—The important symptom of constipation is the infrequency of evacuation or the inspissated character and reduced amount of feces. There is usually a tendency to the formation of hardened masses or scybala. The act of evacuation is attended with difficulty and not rarely with a certain amount of local pain. When the condition is long continued and the masses are of unusual hardness, some mucous coating and even blood-streaked mucus may be observed. If the lower bowel has become impacted, cramps or colicky pains may, for some time, precede the evacuation. Not rarely a certain amount of tenderness is found in the left iliac fossa over the sigmoid flexure.

Various subjective symptoms are met with in persons suffering from habitual constipation, and it is at times difficult to determine how far these have resulted from the condition, or, on the other hand, the degree in which they may have acted as causes of the sluggishness of the bowel. Among such symptoms, heaviness, sleeplessness, a tendency to vertigo, headaches, and even more severe nervous symptoms, like hypochondriasis, may be mentioned. Undoubtedly all of these may be occasioned by the existence of obstinate constipation, but, on the other hand, sluggishness of the bowels is frequently the result of such nervous conditions and perhaps more remotely of the gastric disorders that have occasioned these symptoms. Some authors have suggested that neurasthenia is frequently caused by atonic conditions of the bowel, with more or less constipation, but more commonly constipation is rather a symptom of the neurasthenia than the reverse.

Local abdominal symptoms are common and significant. A feeling of fulness or of pressure, a sense of distention, and sometimes vague or acute pains may occur. Pain may be localized to regions where accumulated masses of hardened feces have caused irritation or inflam-

matory conditions. In other instances cramp-like colic affecting the region of the descending colon or the entire abdomen may result from impaction and from the resulting stimulation of violent peristalsis.

Rectal impactions occasion sensations of bearing down or perineal fulness and even violent tenesmus. Secondary disorders of digestion, with loss of appetite, coating of the tongue, sleepiness, thirst, and sometimes more acute symptoms, such as nausea and vomiting, may, from time to time, make their appearance or be more or less constant.

Fever may occur, when the constipation is temporarily more marked than usual. This may be the result of the irritation of retained material or be the consequence of the absorption of products of decomposition (stercoremia). The evidence in favor of the latter is rather insufficient, as the indications of intestinal fermentation or putrefaction are rarely marked in constipation, and other signs of toxemia are wanting.

Local disorders of various sorts may be encountered, such as palpitation of the heart, irregularity of cardiac action, and various nervous symptoms, some of which have been already mentioned. These symptoms, like fever and cerebral manifestations, have been attributed to auto-intoxication, although the evidence in favor of this view is scanty and uncertain.

The abdomen is sometimes flat or even scaphoid from general contraction of the intestines and insufficiency in the contents of the bowel. More frequently there is slight distention with excess of tympany in the sides due to dilatation of the large bowel. When the abdominal walls are weak and thin, the dilated colon may be seen almost throughout its entire course. Hardened fecal masses may be palpable through the abdominal walls, especially in the sigmoid region. The character of the masses is recognized by their movability, by their disappearance after purgation or the use of enemata, and, according to Gersuny, pressure upon the fecal tumor causes a characteristic sensation of separation of the wall of the bowel from the tumor when the pressure is relaxed. Sometimes fecal accumulations occur in the transverse colon or even in the cecum, and may be very misleading in their resemblance to abdominal tumors.

Occasionally attacks of *diarrhœa* may occur in persons subject to habitual constipation. Such attacks may result from irritation caused by impaction or excessive retention of the intestinal contents from food irritation, or other forms of irritation (purgatives), which act excessively on account of the retention of fecal matter and its hardened character. In cases of fecal impaction in the rectum the real condition may be obscured by a continuous diarrhœa caused by irritation.

The general condition of the patient suffering with habitual constipation may not be seriously impaired. In some cases, however, emaciation, loss of strength, and some anemia may result from the gastric disorders that usually attend constipation, from the constant use of purgative medicines, and possibly from obscure toxic conditions.

Complications.—Among the intestinal complications are dilatation and pouching of the rectum and sigmoid flexure, formation of diverticula, volvulus, and inflammatory lesions in various parts of the bowel (rectum, colon, appendix). Constant straining in constipation may lead to weak-

ening of the abdominal wall and to the formation of hernia. The same cause, together with the pressure of masses accumulating in the rectum and the direct irritation occasioned by hard scybala, frequently leads to the development of hemorrhoids. Severe straining sometimes occasions thoracic diseases, such as emphysema of the lungs. Apoplexy may result from the elevation of blood-pressure caused by severe straining.

Auto-intoxication.—The question of intestinal auto-intoxication has been the subject of controversy for many years; and much clinical and experimental evidence has been collected on both sides. The constituents of the digestive fluids; the products of protein decomposition especially indol, skatol, and histamine; and the synthetic products of bacterial activity have all been suspected of being absorbed and exerting toxic action on the organism. Alvarez,[1] in a recent review of the subject, questions the adequacy of the experimental and clinical support of such a view, and states his belief that many of the symptoms of the so-called "syndrome of constipation" (mental torpor, malaise, coated tongue, and anorexia) may be produced reflexly by the pressure of feces in the lower bowel, and by reverse peristalsis, and may be relieved by evacuation of the bowel in a shorter time than would be required for the elimination of a toxin from the system.

It certainly seems undeniable that there is at times absorption of toxic material from the bowel in adults, as well as in children, whose intestinal mucosa seems more permeable; but further carefully controlled investigation is necessary before final conclusions can be drawn concerning the importance of intestinal intoxication.

Diagnosis.—This usually offers no difficulty, as the infrequency of the evacuations and their character are distinctive. Sometimes, however, there may be daily evacuations of comparatively normal amount, and apparently normal in other respects, in which a test made with the use of charcoal or carmine will show that the time between the ingestion of a certain meal and the discharge of the residue is considerably prolonged. The recognition of such cases might prove difficult, if one did not recognize the possibility of such an occurrence. Fulness of the abdomen, general sluggishness, a tendency to headaches, digestive disturbances, oppression, and other similar indefinite symptoms, may suggest the existence of such latent constipation; and this may be suspected, also, in patients with visceroptosis.

Another direction in which the diagnosis of constipation frequently offers difficulties is in the determination of the *cause* of the condition. The existence of distinct gastric symptoms antedating the tendency to constipation may suggest that digestive disturbance is mainly operative. A study of the patient's diet may bring out that a too monotonous diet, or one lacking in fluid elements, or, on the other hand, foodstuffs that by irritation provoke intestinal spasm, lie at the basis of the condition. The condition of the abdominal walls, a tendency to gaseous distention, and other indications of sluggish peristalsis, may show that constipation has resulted from intestinal atony. Hemorrhoids or fissure, pelvic

[1] *Phys. Rev.*, July, 1924, **4**.

diseases, displacements of the uterus, or the presence of abdominal tumors, may indicate that the disorder has resulted from reflex atony or spasm of the bowel; or, in other cases, from direct pressure upon it. Finally, general nervous conditions, such as neurasthenia or other depressive conditions, may suggest the importance of the nervous system in the etiology. In these instances careful consideration of the possibility that the nervous conditions are secondary to the constipation must be remembered in attempting to determine the sequence of events.

No satisfactory treatment can be instituted until the proper causation has been investigated and determined.

Treatment.—The most important element is the establishment of the habit of regularity in the evacuation of the bowels. The normal regularity is due to fact the that the feces reach the lower bowel at a certain interval after the ingestion of food, and there stimulate the mucous membrane and bring about a desire for evacuation. A habit of resisting this desire may gradually cause a blunted sense, which eventually occasions more or less obstinate constipation. A process of reëducation is frequently effective, and the most natural and desirable method of treatment is the establishment of a habit of regularity. For some time no result may be achieved, but repeated efforts at a certain hour—preferably that which seems to be the normal time (that is, the morning)—will gradually prove effective. In some cases it seems desirable to choose the evening rather than the morning, especially when local rectal conditions, such as hemorrhoids, are present. The retention of fecal matter in the lower bowel during the night may occasion a reflex spastic constipation.

Simple measures may be used to supplement the effort at reëstablishing the normal regularity. Among these the use of small enemata of plain water or soapsuds, with or without the addition of a little glycerin, and glycerin, gluten, or soap suppositories, may be recommended. All such aids should be used with caution, as the bowel readily accustoms itself to artificial assistance.

Exercise.—Exercise of the abdominal muscles in particular is important, although the muscular system as a whole must be considered, since its normal healthful condition has a bearing upon the function of the bowels as on other visceral functions. The form of exercise must vary according to the physique, character, and occupation of the patient. In many, gymnastic movements and the use of pulley weights, rowing machines, or other apparatus that will enable the patient to obtain vigorous exercise, particularly of the muscles of the abdomen and trunk, answer the purpose. In others, a better result is accomplished by directing the patient to occupy himself with such labors as will secure the proper amount of exercise. In obstinate cases, passive exercise or massage must be employed. The patient may knead the abdominal muscles along the course of the large intestine, or may use a cannon ball covered with felt or leather, which is rolled about the abdomen. The weight of the ball may vary from 2 or 3 to 10 pounds. Various implements have been devised for producing vibrasage, and these may give good results. Active stimulation over the cecum and sigmoid, and a continuous treatment along the line of the large intestine, give the best results. Sometimes it is well

to combine with the manipulations of a masseur injections of plain water.

Electricity and hydrotherapy have been used; a slowly or rapidly-interrupted faradic current may be applied over the colon, beginning at the cecum, and following the entire length of the large intestine. Galvanism has also been employed, the current being interrupted from time to time. Ordinarily one electrode is placed under the back, while the other is applied to the surface of the abdomen.

Baths of various sorts have been employed to stimulate the abdominal muscles, as well as the intestinal peristalsis. Cold douches, wet compresses to the abdomen, and general hydrotherapy may be useful.

Diet.—It is impossible to make any general statement regarding the character of diet that should be prescribed for patients suffering with this condition. In general, it may be said that such forms of food as furnish a considerable amount of residue are likely to prove useful, while those foods which are susceptible of complete digestion and absorption tend to occasion constipation if they form too large a proportion of the whole dietary. It has, therefore, become customary to prescribe for patients with constipation various vegetable foods that leave a large residue. Other things bring equal, this plan proves satisfactory; but sometimes unabsorbed portions of food may act as irritants and tend to increase the condition. In the same way, fruits, berries, and the like, which contain seeds or other non-absorbent constituents, may be helpful or hurtful, according to the nature of the case. All kinds of fruits have been advised and frequently aid in combating the trouble. Sometimes, by causing disturbance of gastric digestion, fruits may have an opposite effect. Sweets, honey, milk-sugar, and other saccharine or carbohydrate foods sometimes prove efficacious. Stewed fruit at night, or a few dried plums, may have a useful effect. Milk-sugar has been largely employed in the same way.

The regular administration of water in increased amounts, and especially one or two glasses of hot or cold water before breakfast, may be helpful. Certain inert substances, such as agar-agar, which swells from imbibing water and is not digested or absorbed, liquid paraffin or petrolatum, are sometimes taken with advantage. The use of olive oil in doses of from a teaspoonful to an ounce after each meal is sometimes effective. Various kinds of bread made of coarse flour or containing bran may supply a certain degree of desirable irritation. Certain foods have a recognized constipating effect. Acid wines or tea, on account of the astringent effect of the constituent tannic acid, are undesirable. Milk is usually constipating, but only when it forms a considerable portion of the whole diet, and when, as a rule, the amount of residue is insufficient.

Medical Treatment.—Medicinal agents should be used only when a regulation of the daily life of the patient, or of his diet, and the employment of various physical means of stimulating peristalsis have failed of the desired result. Undoubtedly, the common cause of increasing constipation is the employment of remedies without reference to the individual conditions, and usually without medical advice. Often, however, some kind of direct medical treatment seems necessary, and drugs may

be required. These may be divided into those which exercise a helpful influence on digestion and peristalsis, without having a direct laxative effect, and those which are laxatives in a narrower sense.

Among the remedies that are correctives of digestion and stimulate peristalsis without irritating, nux vomica, belladonna, physostigma, and digestive ferments may be considered. In some cases a small dose of tincture of belladonna may suffice to aid the condition.

Of the *direct laxatives*, aloes and cascara are probably most generally useful. The combination of aloes with belladonna and strychnine in pill form is useful, and if carefully controlled by other measures rarely requires such increases in the quantity of the remedies as to make it distinctly undesirable. Aloes may also be combined with podophyllin, extract of rhubarb, or cascara. Cascara, in the form of the fluidextract or solid extract, or of various elixirs, is a favorite remedy, and does not seem to increase the tendency to constipation. It is difficult to determine without experiment the required dose, individuals differing very widely. The combination with aloes or other purgatives often acts more happily than the drug without addition. Phenolphthalein is often useful and may be given with cascara. Recently combinations of agar, phenolphthalein and paraffin oil have come into use.

Senna is widely used and forms the basis of many proprietaries. An old practice is to administer stewed prunes, to which a few leaves of senna have been added; and senna teas, decoctions, etc., are extensively used. The official confection of senna, or one containing senna, rhubarb, sulphur, and glycerin, taken before bedtime, may be used. Sulphur may be used as a laxative, although its potency is rather limited.

Saline waters of various sorts, such as those of Marienbad, Carlsbad, Bedford, or Saratoga, may be useful. One or two drams of saturated solution of magnesium sulphate or Rochelle salt have a similar effect. As a rule, these waters are most efficacious when taken before breakfast or at night. The continued use of waters in regulated amounts may have a permanently useful effect, correcting digestion or catarrhal conditions of the gastro-intestinal tract, but the unrestricted use of any kind of saline water must be condemned.

Rectal medication is often highly beneficial, and in cases in which some form of remedial agent seems to be necessary, the substitution of enemata, suppositories, etc., for remedies given by the mouth has the effect of preventing the development of a habit. The habit of employing enemata regularly or daily is quite common with some persons. It is not harmless, as the effect upon the mucous membrane of the lower bowel sometimes proves distinctly deleterious. As temporary expedients, enemata of plain water, saline solution, soapsuds, or more powerful combinations, such as solutions of sulphate of soda, Rochelle salt, or other salines, may be employed. In some cases, the injection of a small quantity of olive oil at night, to be retained until morning, has a useful effect, particularly when larger enemata are irritating. In spastic constipation, such injections of oil or enemata of large quantities of oil may be employed. The addition of glycerin to enemata renders them more powerful, and especially efficacious in acute cases. The periodic use of

colonic irrigations with plain water, saline solution, or variously medicated solutions has enjoyed an increasing popularity.

Sedatives may be useful in the treatment of constipation when the condition is more or less dependent upon spastic states of the bowel. In these circumstances the milder sedatives, such as bromides, valerian, and especially asafœtida, given in the form of pills, each containing gr. ij, (gm. 0.13), or administered by enemata in the form of milk of asafœtida, serve a useful purpose.

Some attempts at correcting constipation due to a deficiency of microbic action have been made by the employment of cultures of microörganisms, such as *Bacillus acidophilus*.

Surgical Treatment.—Attempts have been made to correct constipation by eliminating the large bowel from the intestinal tract. Among others, Lane has practised anastomosis of the small intestine with the sigmoid flexure or the rectum. Complete removal of the large intestine has been practised, but is obviously too radical a procedure to warrant recommendation. Even the more conservative forms of surgical treatment are justifiable only in cases of unusual obstinacy.

IDIOPATHIC DILATATION OF THE COLON

This term is used to define certain cases of more or less extensive and persistent dilatation of the colon, probably dependent upon structural abnormalities, and not due to ordinary obstructions and to consequent accumulations of gaseous or fecal contents. The cecum, colon, and sigmoid may be enormously distended throughout their entire lengths. In some cases the sigmoid alone is involved, and may be so greatly enlarged that it fills the entire abdominal cavity, pressing other viscera out of the way. The diameter of the bowel may reach as much as 8 or 10 inches. When the colon is involved, the abdomen is filled with the enormously distended colon, occupying either half of the abdominal cavity, which is so greatly enlarged that the patient presents the appearance of a monstrosity. Fornad's celebrated case was exhibited in various places under the name of the "balloon man."

Etiology.—A distinction may be made between cases in young children and those in the elderly or aged. The former group probably represents cases in which some congenital defect is the occasion of the dilatation, which gradually progresses. In the cases occurring after childhood, contributing causes, such as partial obstruction, habitual constipation, and weakening of the bowel by chronic inflammatory affections, probably more frequently play a part. In a case reported by Treves the dilatation was due to congenital narrowing of the rectum; and this author concluded that idiopathic dilatation is usually due to obstruction with resulting fecal impaction. Marfan suggested that a congenital abnormality in the form of the sigmoid flexure might be the cause, and a number of cases have been described in which the sigmoid was abnormally long and therefore distorted. Other causes of impediment in either the sigmoid or the rectum may occasionally play some part in the causation. Some form of muscular weakness of the entire bowel has been assumed as the

basis; but idiopathic dilatation is not the result merely of atony of the bowel, as the walls are invariably found hypertrophied.

The important features are the great distention, a thickening of all the coats of the bowel, and especially hypertrophy of the muscle. The mucosa is usually swollen, congested, and ulcerated. As a rule, it contains large quantities of fecal matter; in Formad's case the contents of the colon weighed forty-seven pounds.

Symptoms.—The most conspicuous feature is the abdominal enlargement, which is due largely to gaseous contents. The distention may be uniform and globular, or more on one side—particularly on the left side—when the sigmoid is specially involved. The coils of intestines may be visible through the abdominal wall, and peristaltic waves may be seen. Interference with breathing and with the circulation is commonly the result of the upward displacement of the diaphragm. The patient complains of abdominal distress, but acute pain is usually wanting. Gastric disturbances, headaches, and intense constipation are usually encountered. Sometimes there are paroxysms of colicky pain, and occasionally attacks of diarrhœa may set in, especially toward the end of life. In some instances the bowels have been regular throughout, although there was nevertheless a gradual accumulation of retained fecal matter. The patient suffers with increasing malnutrition, which finally may become extreme; and death may be due to inanition and exhaustion. In other cases a fatal termination is due to volvulus of the sigmoid or to perforation of the bowel. Sometimes the fatal result appears to be due to the extensive associated colitis.

The clinical course in *congenital* cases begins within the first few days of life. The abdomen begins at once to enlarge, and increases progressively. At the same time, obstinate constipation attracts attention, practically no fecal matter being discharged, except at long intervals. In some cases a history has been obtained that the child had had but few bowel movements since birth, although some months or a year or more old. The child usually dies early; in Griffith's series only three out of twenty-four cases reached adult years. In other cases the symptoms do not begin until a year or more after birth. Milder forms and sometimes even extreme cases may go on to adult or middle life.

Treatment.—In some cases the administration of purgatives may cause evacuation of retained contents; but this is followed by a speedy recurrence and is attended with little relief, even for a time. The same unsatisfactory result attends the use of enemata. In a number of cases surgical treatment has been employed and in some has been followed by satisfactory results. The operation most generally employed has been colostomy. More extensive operative procedures, such as excision of parts of the bowel, have been resorted to with variable results. Richardson's case, in which excision of the sigmoid flexure was followed by the formation of a new sigmoid, is instructive in illustrating that inherent structural defects may lie at the basis of the etiology in some instances. Probably in most cases operation has been undertaken too late.

Redundancy of the Colon.—In this condition, which has been brought into more prominence by the development of roentgenologic diagnosis,

the colon is too long, falling into loops and kinks, and often has a long mesentery. The redundancy may be general in the colon, or localized to a particular area; when the latter is the case the sigmoid colon and splenic flexure are most often affected. It is usually thought to be congenital, but may conceivably be the result of chronic overloading in constipation, or the abuse of cathartics.

Symptoms may result from periodic filling up of the redundant bowel; prominent among them are constipation (occasionally associated with fever and systemic symptoms, and followed by copious evacautions), periodic abdominal distention with pain or distress, and occasionally reflex gastric symptoms. Acute obstruction from volvulus has been reported.

Roentgenologic examination with the aid of opaque media is necessary for diagnosis. The treatment should be directed toward preventing stasis in the redundant bowel by the use of a bulky diet, lubricants or colonic flushings.

DIARRHŒA

Definition.—The term diarrhœa is usually applied to the too frequent discharge of more or less fluid stools. In many persons two or three daily evacuations of the bowels occur without disturbance of health, and without any marked alteration in the character of the feces from the normal. This does not constitute diarrhœa in the ordinary acceptance of the term. Usually, however, when more than one daily movement occurs, the feces are also less solidified; and although active symptoms may be wanting, the condition is really diarrhœa.

Etiology.—As the essential condition is the presence of an abnormal amount of water in the feces, the causes will be found to be such as occasion the rapid evacuation of the intestinal contents, with consequent reduction in absorption or an oversupply of water or increased secretion from the mucous membrane of the bowel.

The forms of diarrhœa may be classified as those without definite organic lesion and those associated with various intestinal diseases. In the latter group the condition is symptomatic, and more appropriately considered in connection with the various diseases that cause it.

Diarrhœa Due to the Excessive Ingestion of Water and Other Fluids.—Sometimes the mere drinking of excessive quantities of water may be the cause of looseness of the bowels. In some individuals in whom there is usually a constipated condition excessive water drinking may correct the difficulty or even produce a temporary diarrhœa. The drinking of other fluids, such as malt liquors, etc., may act in the same way, although there is probably here an associated cause, the digestive disturbance resulting from the overuse of the fluids. Diarrhœa is sometimes produced by the use of large quantities of oil, butter, or fatty food. In this case the amount of unabsorbed fat may occasion looseness, or digestive disturbance may result from the excess of fat consumed, and the fatty acids or other products of decomposition may act as irritants.

Diarrhœa Due to Food.—Various foods may occasion diarrhœa, through their mechanically irritating character, through their ready decom-

position in the gastro-intestinal tract, and sometimes through their mere bulk. It is well known that fresh fruits, certain vegetables containing abundant cellulose, and berries containing small seeds may, in some individuals, readily provoke an attack of diarrhœa that can be explained by the mechanical irritation occasioned by the unabsorbable residue. Other foods, such as fish, shell-fish, cheese, milk, etc., may easily undergo decomposition in the bowels or may contain preformed products of decomposition, particularly in hot weather, and thus may excite more or less acute or violent diarrhœa. Various microörganisms have been found in association with cases of this sort. Mere excess of food may set up a diarrhœa as a result of derangement of the gastric and upper intestinal digestion and secondary bacterial fermentation.

Diarrhœas Due to Purgative Substances.—Any of the various purgatives used in practical medicine may occasion active diarrhœa. The majority of these act upon the muscle of the bowel and its nervous mechanism without influencing the secretions or absorptive processes. Their effect is simply to stimulate peristalsis, especially that of the large intestine. The salines increase watery secretion from the intestinal mucous membrane; and some exercise a stimulating effect upon peristalsis.

Diarrhœa Due to Nervous Influences.—A variety of conditions may excite increased peristalsis by directly affecting the nervous mechanism of the bowels. The influence of shocks, fright, fear, and various kinds of excitement, is well known. In some diseases attended with disorders of the nervous system, like Graves' disease, hysteria, or neurasthenia, attacks of diarrhœa or continued looseness of the bowels may occur. In some persons the nervous mechanism of the intestines appears particularly susceptible, and slight influences, such as emotional conditions, exposure to cold, or various forms of irritation ordinarily having little effect, may readily increase peristalsis. The condition known as *morning diarrhœa*, in which several evacuations occur in the early morning, after which the bowels remain quiet until the next day, may be explained by an irritable state of the nervous mechanism in the lower bowel, and the consequent prompt evacuation of contents that usually reach this portion of the tract twenty-four hours after the beginning of ingestion.

Diarrhœa Due to Diseases of Other Organs.—In some cases of heart disease, congested conditions of the mucous membrane of the bowel may occasion a proneness to diarrhœa, or may cause it directly by increasing intestinal secretion. The association of diarrhœa with renal disease is most important. The vicarious excretion of urea from the intestinal mucous membrane and the decomposition of this, with the production of ammonium, occasion irritation, sometimes of intense character. In all cases of severe kidney disease the development of diarrhœa must be regarded with suspicion.

More or less intense diarrhœa may be associated with various infections not necessarily involving the intestinal tract itself. Thus, in cases of septicopyemia and pneumonia, and in various other infections with lesions at a distance from the bowel, diarrhœa may occur. There is reason to believe that such attacks are due to the elimination of toxic matters from the intestinal mucous membrane, just as urea is eliminated

in cases of disease of the kidneys. It has been shown that the toxins of such organisms as the *Bacillus dysenteriæ* injected hypodermically may be eliminated through the bowel, causing secondary lesions of the mucous membrane. The same is true of injections of cholera toxin. Even in infections of the intestinal tract, therefore, such as cholera, dysentery, etc., the attending diarrhœa may be due to the toxic state of the blood and the secondary elimination of the toxins through the mucous membrane of the bowel.

Diarrhœa of Gastric Origin.—In certain diseases of the stomach, especially in achylia gastrica, a tendency to diarrhœa may be a marked feature. In achylia this has been attributed by some to the absence of free hydrochloric acid and consequent failure of the normal anti-bacterial action of the gastric juice or to the rapid passage of poorly digested food through the relaxed pylorus, while others believe it results from the lack of sufficient stimulus for efficient pancreatic secretion and consequent failure of digestion. The offensive character of the stools and the presence of large numbers of bacteria lend some color to the former view, while the amount of undigested food residue, especially meat fibres, supports the other view.

Diarrhœa may also occur in cases of marked hyperacidity of the stomach, though in this case it is usually only a temporary occurrence in persons usually constipated.

Diarrhœa Due to Intestinal Indigestion.—Certain persons are liable to attacks of fermentative diarrhœa apparently of intestinal origin and particularly after taking some particular kind or kinds of food. The gastric conditions are found to be normal, but distention, colicky pains and the passage of fermenting, highly offensive and acid stools of a crumbly character occur during the attacks. At times this condition is quite obstinate. The stools are often light from admixture of gases of fermentation and float in water; they may be light yellowish or brownish in color and contain abundant microörganisms of fermentation.

Diarrhœa Due to Organic Diseases of the Bowel.—In connection with enterocolitis and other catarrhal and inflammatory conditions of the mucous membrane, in the descriptions of the various ulcerations of the bowels and of malignant disease, diarrhœa will be discussed.

Bacteriology of Diarrhœa.—Bacteria and their products are sometimes the direct causes of diarrhœal conditions. A considerable variety of microörganisms may be concerned and it is difficult to determine with certainty in many cases which of the abundant intestinal flora is mainly operative. Certain facts have been learned by observations of the predominant organisms in different cases, by the discovery of forms in abundance that normally are not present and that have been traceable to tainted food, and by the application of agglutination tests to the serum of individuals suffering with diarrhœa.

Certain of the normal organisms of the intestines to which the system has grown accustomed may undergo unusual multiplication or increase of virulence, so that they become pathogenic. Among these the *Bacillus coli* is most important. The fact that this organism is largely present in cases of diarrhœa does not necessarily imply its etiological relation. There

is little doubt that under some conditions diarrhœal diseases are caused by this group of organisms.

Closely allied organisms, such as the *Bacillus enteritidis* of Gaertner, and members of the intermediate group, the paratyphoid and paracolon bacillus, are important causes of certain diarrhœal conditions. Diarrhœa due to the *Bacillus enteritidis* has been found in some cases of meat poisoning and sometimes also in cases not directly traceable to the consumption of tainted meat. In some cases, especially in the diarrhœas of childhood, streptococci and staphylococci appear to be the active agents and may cause intense enteritis. Among less frequent causes are various other organisms inhabiting the intestinal tract normally, which may operate by their direct action or by causing fermentative processes with the liberation of fatty acids and other irritant substances that secondarily occasion intestinal disturbance and diarrhœa. In the disorders of intestinal fermentation, organisms of fermentation may be conspicuous—among these the clostridium butyricum or granulo-bacillus, saccharo-butyricus, and long bacilli (Oppler-Boas?), *Bacillus pyocyaneus*, Friedländer's bacillus and other forms occur more rarely. Certain organisms of specific diseases, such as typhoid fever, tuberculosis, etc., occasion characteristic lesions and often an associated diarrhœa.

Diarrhœa is sometimes occasioned by protozoa, including amœbæ and a variety of flagellate and ciliated forms, as well as the helminth group.

Symptoms.—The clinical manifestations of diarrhœa depend largely upon the nature of the condition and the part of the bowel involved. In cases of irritation of the *upper* intestine due to overloading with food or functional derangement, diarrhœa may not occur if the peristalsis of the colon remains normal; but usually an increase of activity occurs in this part of the tract as well, and some looseness results. In such cases the stools are likely to present features that indicate the upper bowel to be at fault. Undigested food, with the admixture of considerable mucus, rendering the feces pasty, sticky, or viscid, and a yellowish or greenish coloration, due, in part, to unaltered bile and largely, often, to pigment derived from bacterial action, are characteristic. Excessive acidity may render the discharges highly irritating and occasion inflammatory conditions of the rectum, anus, or even of the skin externally. This is common in diarrhœas of this type in childhood.

In cases of widespread irritation of the bowels, involving both the large and the small intestine, more copious watery discharges are the rule. There is usually an admixture of fecal matter, and the color of the movements may vary from a dark brown to a light yellow; or, when abundant serous outpourings occur, as in choleriform types, almost watery discharges are seen.

When the *large* intestine is particularly involved there is usually considerable mucus of whitish color, and more frequently in masses than in cases involving only the upper intestine. It may be seen as jelly-like particles or as large accumulations; and sometimes, alternating with the discharges of ordinary diarrhœal type, the evacuation of almost pure mucus or mucus streaked with blood may be encountered.

The subjective symptoms in cases of moderate diarrhœa may be very slight. As a rule, when the small intestines are involved, colicky pains and abdominal tenderness are usual. These may be intense, and the patient may become prostrated from the severity of the pain, as well as from the loss of water and other causes. In cases of diarrhœa involving special irritation of the lower bowel, local tenderness in the left flank or above the pubis may signify involvement of the descending colon and sigmoid. In these cases, tenesmus is not unusual.

Soon after the onset of diarrhœa a certain degree of weakness or prostration is usual. In mild cases this is of little consequence. In severe forms extreme prostration or collapse may occur. The circulation becomes enfeebled; a little cyanosis may be present; and in children, sinking of the eyes and fontanelles, pinched features, and other indications of the Hippocratic facies are seen.

Fever is rarely found in mild cases, but slight elevations are not unusual in the more severe. On the other hand, the prostration may be such that the temperature soon becomes subnormal.

Disturbance of the stomach sometimes attends diarrhœa, either as a result of the original dietary disturbance or other irritation that has occasioned the diarrhœa, or as a reflex result of pain and irritation.

The clinical *course* of cases of diarrhœa varies with their cause and nature. In ordinary instances due to digestive disturbance a few evacuations succeeding each other at intervals of a half hour to several hours may terminate the condition. In more severe cases, and particularly when more intense irritation of the intestines has occurred, the diarrhœa may increase in severity for a day or two, or may reach its maximum only after several days. In such instances the stools tend to become more and more watery as the contents of the bowel are evacuated, while in cases in which the large bowel is involved there may be, in the later stages, only discharges of mucus. In most instances the entire duration is not above several days, unless secondary enteritis or colitis has complicated the condition.

Diagnosis.— This is mainly concerned with the recognition of the cause. Ordinary diarrhœa must be distinguished from various forms of specific intestinal disease or general infections accompanied with intestinal manifestations.

Treatment.— Prophylaxis is of great importance. The avoidance of irritating or tainted foods, particularly during hot seasons of the year when decomposition is apt to occur, is the most important measure. Uncooked fruit, shell-fish of various sorts, berries, and cold drinks are among the articles of diet to be scrutinized with greatest care. Residents of hot climates have found it advantageous to wear an abdominal band of flannel or some woven material, to secure warmth and protection, particularly when cool nights succeed hot days. Local applications of heat over the abdomen, in the form of hot-water bags, hot fomentations, and binders of various sorts, are often quieting in the onset and may moderate the severity of the attack by controlling peristalsis.

Diet.— The diet during an attack of diarrhœa should be extremely moderate in the beginning, and often it is necessary to avoid food

altogether. Later, and particularly in cases in which prompt control is not secured, a cautious increase of food is requisite, lest the patient's strength be too greatly impaired. Thirst, which may be complained of severely, should be controlled by the swallowing or eating of small bits of ice and the sipping of small amounts of cold water. Frequently, merely holding water in the mouth is satisfying. Albumin-water, barley-water, rice-water, or toast-water may be used to quench thirst and, at the same time, to supply a certain amount of nourishment. If the stomach is irritable, these liquids may be better tolerated than plain water. After preliminary evacuation of the bowels has been secured, a diet of pasteurized or boiled milk, given in small quantities, or milk with well-cooked farinaceous foods, such as arrow-root, rice boiled in milk, milk toast, etc., may be given. Later soft-boiled eggs, gelatin preparations, such as meat jellies, and, still later, scraped beef or minced chicken, may be allowed. It is usually advisable to avoid giving vegetables until the signs of gastro-intestinal irritation have subsided.

Medicinal Treatment.—After the onset, the first consideration in the treatment is the evacuation of irritating material, if the spontaneous discharges are not enough to carry these off. Nearly always it is desirable to use some unirritating and rapidly acting purge, such as castor oil. It is a common practice to add to this a small amount of tincture of opium or paregoric, to allay irritation and prevent unnecessary griping. Other purgatives, such as calomel, salines, magnesia, and the like, may be used instead of castor oil; but they are less prompt in their effects. After evacuation of the irritants the use of sedatives is desirable. Bismuth powders, to which may be added pepsin, if digestive disturbances are present, chalk mixture, cerium oxalate, lime-water, or other alkalis may be used to quiet intestinal irritation and neutralize acidity. A combination of chalk mixture with paregoric and some astringent, like tincture of kino or catechu, is frequently used.

When cramp-like or colicky pains are present, some form of sedative and carminative may be added or substituted for the remedies named. Chlorodyne or improvised mixtures containing other carminatives, such as spirit of chloroform, compound tincture of cardamom, or spirit of ginger, with opium, may be employed for this purpose. When intense pains occur and collapse threatens, the timely use of a hypodermic injection of morphine, followed by the various remedies already named, may cut short an attack that promises to be serious. Sometimes suppositories of opium may be substituted for these, or repeated doses of paregoric or of tincture of opium may be given by the mouth.

Sudden diarrhœas, attended with marked evidences of intestinal irritation, should be treated with promptness; and active remedies, astringent, sedative, and protective, should be given early. As a rule, the evacuations are so free that little is gained from a preliminary administration of purgatives; and these may, at times, be actually harmful. Bismuth in fairly large doses (gr. xxx, gm. 2), in the form of the subnitrate, subgallate, or salicylate, with vegetable astringents, such as kino or catechu, repeated doses of opium, and an occasional hypodermic of morphine, may be given. Mineral astringents sometimes

have a greater controlling effect than the vegetable forms. Small doses of subacetate of lead or nitrate of silver may be employed.

When diarrhœa becomes obstinate or chronic, persistence in the use of the same kind of treatment, using small doses of the various drugs named, will gradually control the disorder. Diet here, however, plays a more important rôle than does the medicinal treatment. No general rules can be laid down regarding the most desirable diet, as individual peculiarities play an important part and therefore require individual consideration. In most cases the use of pasteurized or boiled milk, with or without small amounts of farinaceous food, proves most suitable. In some persons, however, milk is not tolerated; and even forms of food prepared with milk may protract the diarrhœa. In such individuals, eggs and rare meat, with a farinaceous diet, may prove more acceptable. Occasionally the use of some astringent water, like the Rockbridge alum water, aids in controlling a persistent diarrhœa.

Nervous diarrhœas are best treated with remedies directed to the general nervous system and careful regulation of the diet, so that any undue taxing of the digestive functions may be obviated.

Diarrhœa attended with irritation of the lower bowel sometimes requires local treatment. In the acute stages, if tenesmus, pain, and other local symptoms are marked, relief may be obtained from ice suppositories or from the injection of small quantities of cold water or larger amounts of starch water containing tincture of opium. When a residual catarrhal condition persists, the cautious use of colonic injections of weak solutions of nitrate of silver (1 to 5000) may be useful; but repeated injection and stronger solutions may easily do harm.

ACUTE ENTERITIS

Definition.—This term may be employed to designate acute catarrhal inflammation of the mucous membrane of the small intestine as well as the upper portion of the large bowel. The terms acute inflammatory diarrhœa, enterocolitis, and ileocolitis are synonymous with that here preferred. It is impossible to distinguish this condition sharply from irritative diarrhœas due to digestive disturbances and certain infectious diseases with intestinal manifestations. In the former group are cases in which actual enteritis results from the highly irritating character of products of intestinal fermentation. In the latter group are many infections often situated at a distance from the intestinal tract, in which complicating enteritis results from irritating toxins in the blood, excreted into the bowel. There are also the specific infectious diseases, such as typhoid fever, dysentery, etc., in which enteritis is an important lesion.

Etiology.—Individual susceptibility often plays a part, certain persons being exceedingly liable to this form of disease. Enteritis is more common in hot weather and in hot climates than at other times or elsewhere, owing to the greater likelihood of the contamination of food in these circumstances, and because certain easily tainted foods like fruit are more commonly used. As in childhood, chilling of the surface during cool nights following hot days plays some part in the etiology.

The direct cause is usually some chemical irritant contained in food. The irritants, however, may reach the intestines through the circulation. They are quite varied, depending upon the character of the food, its preparation, and its preservation. Sometimes, although wholesome when swallowed, excessive quantities of food or digestive disturbances may occasion fermentation in the intestinal tract and the formation of irritants that directly excite a catarrhal inflammation. *Bacteria* probably rarely cause catarrhal inflammation directly. Usually their relation is that of agents causing fermentative changes and the products of such fermentation are the immediate causes of the enteritis.

Among other causes of enteritis must be named mineral poisoning, or poisoning by toadstools or other noxious substances. Overdoses of lead, mercury, arsenic, copper, and other mineral substances may occasion intense forms of enteritis with violent symptoms.

Pathology.—The mucous membrane of the bowel may be involved with almost equal severity from the stomach to the upper portion of the large intestine, but usually certain areas are more seriously implicated than others. The mucosa is swollen and reddened. Often the crests of the valvulæ conniventes alone present an inflammatory appearance. The surface is usually covered with mucus, which may be blood-tinged, and sometimes hemorrhagic extravasations occur in the mucosa. The lymphatic follicles are swollen and stand out prominently as light areas against the inflamed surface. The Peyer's patches may be swollen, and occasionally show small rounded ulcerations.

In exceptionally violent forms, pseudomembranous or diphtheritic inflammation of the mucous membrane of the small and large intestine may occur. Sometimes this is primary, in the sense that no preceding infective lesion can be discovered; but much more commonly it is secondary to infections originating elsewhere. The same form may be met with in cases of chronic nephritis or uremia, following cirrhosis of the liver and other conditions producing portal obstruction, and in association with obstructions of the bowel caused by carcinoma or other lesions. Sometimes an intense enteritis with pseudomembrane formation occurs as the result of mineral poisoning, such as is caused by mercury.

Symptoms.—The clinical manifestations vary with the intensity of the cause and the part of the intestinal tract principally affected. In milder cases the symptoms are those of ordinary diarrhœa due to dietetic errors and functional disturbances. In severe cases the manifestations are sudden and violent.

The *stools*, as a rule, are of ordinary diarrhœic character, liquid, brownish, and more or less offensive, according to the degree of putrefactive change taking place. In the beginning there may be merely pultaceous movements which evacuate the lower bowel; later the movements become more watery, and frequently contain a certain amount of visible mucus. When the large intestine is especially affected, the amount of mucus may become considerable; but in most cases the discharges remain thin, watery, and brownish. When enteritis is due to irritants of great intensity, very frequent and abundant watery movements result; and an excessive diarrhœa, approaching in severity

that of an attack of true Asiatic cholera, may occur. Sometimes constipation instead of diarrhœa is met with in cases of enteritis, the explanation of this being that inhibition instead of stimulation of peristalsis has resulted from the irritation. Undoubtedly many cases of acute constipation following indiscretions in diet and irritation of the upper part of the small intestine are produced in this manner. When actual enteritis is present, and especially when it is extensive, diarrhœa practically always results. In some cases of intense and localized enteritis paresis of the affected segment of bowel may occasion intense constipation or even complete obstruction of the bowel.

The patient usually suffers with colicky pains and more or less abdominal soreness from the beginning. As a rule, this is of moderate severity, but sometimes it becomes extreme. Distention of the abdomen from gaseous accumulations may occur, and loud rumbling or gurgling sounds (borborygmi) are frequently heard. In some cases, owing to great severity of inflammation in a certain restricted part of the bowel, intense pain and tenderness may be found in a localized area of the abdomen. When the lower part of the ileum is involved the local symptoms may suggest appendicitis. In these cases rigidity of the abdominal muscles in the area of pain and tenderness, the occurrence of fever, of vomiting, and of leukocytosis may still further confuse diagnosis. The development of diarrhœa is usually the determining symptom in the establishment of a proper diagnosis, but this may be wanting in enteritis, and in exceptional cases is met with in appendicitis.

In the beginning, irritation of the stomach is usually met with, and vomiting may be a disturbing symptom at the onset. Later, this subsides, as the intestinal symptoms become more pronounced. Some gastric disturbance, however, usually persists. The tongue becomes coated and dry, appetite is wanting, there is more or less nausea or distress after eating, and frequently vomiting is easily provoked throughout the course. When the upper part of the small bowel is especially involved, active gastric symptoms may be a conspicuous feature of the clinical manifestations. Continuous nausea and vomiting and localized pain in the upper part of the abdomen are marked. Sometimes moderate jaundice indicates a special involvement of the duodenum.

Fever is more or less high from the beginning, some elevation of temperature rarely being absent. The temperature bears no relation to the severity of the intestinal manifestation. In extensive enteritis of moderate severity a continuous fever resembling that of typhoid fever may occur, and the diagnosis is therefore at times quite uncertain.

The patient suffers with loss of strength and general debility, in proportion to the degree of irritation and the intensity of the diarrhœa. In cases in which large, watery evacuations are frequently repeated the patient may fall into a state of rapid prostration or collapse. In such instances the surface becomes cold and moist, cyanosis of the extremities may be noted, or there may be complete collapse.

The physical signs, as a rule, indicate nothing beyond a slight abdominal distention, with more or less tenderness on pressure. In some cases, however, marked tympany is observed.

The secretions become scanty, the urine particularly being reduced in quantity, and often presenting a certain amount of albumin with hyaline or granular casts. In intensely infective cases, acute nephritis may occur. Examination of the blood reveals moderate grades of leukocytosis.

In pseudo-membranous enteritis secondary to infective lesions elsewhere, high fever, intense intestinal symptoms, and rapid prostration of strength are usually encountered. The evacuations in these cases may contain shreds of pseudomembrane or of exfoliated mucosa, and sometimes blood and pus.

Cholera Nostras.—Cholera nostras, or cholera morbus, is an intense form of acute enteritis, bearing the same relation to ordinary cases of enteritis of adults as cholera infantum bears to ordinary enterocolitis in childhood.

Etiology.—This occurs with greatest frequency in the summer months, and is usually, although not always, traceable to some error in diet. Probably in many cases bacterial infection plays an important part, although no particular form of organism is associated with it. In some cases, preformed products of bacterial decomposition in the food are active; in other cases it is probable that, as the result of digestive disturbance after errors in diet, bacterial decomposition takes place. Chilling is an important etiological factor. Exposure during cool nights following hot days, and when the surface has been relaxed and moistened by active perspiration, is particularly important.

The pathological anatomy does not differ essentially from that of other forms of enteritis. There is, however, a tendency to marked exfoliation of the mucous membrane and follicular infiltration; and, as the consequence of intense serous outpourings, desiccation and anemia of various organs may be discovered.

Symptoms.—The onset is sudden and violent, usually beginning with nausea and intense vomiting and violent abdominal pain. The patient speedily falls into a condition of prostration from the intensity of the suffering and the violent nausea and vomiting. The contents of the stomach are soon evacuated, after which bilious vomiting takes place; and finally, watery liquid is discharged, or intense unproductive retching may ensue. Soon after the onset diarrhœa begins. After the discharge of the contents of the lower bowel the movements become copious, watery, and frequently repeated. They are discharged without special effort or tenesmus, and may finally become almost or quite involuntary. From beginning to end the tendency to large, watery evacuations is a marked feature.

The abdomen is tender, and sometimes excessively so. The patient in the beginning lies upon the side, with the legs flexed to relieve pressure, or upon the back, with the thighs flexed upon the body. Later, sensation becomes less acute, owing to prostration, and pain and tenderness become less marked. At the onset the temperature rises, and sometimes reaches a considerable degree of elevation. Exceptionally, hyperpyrexia may occur. Later, as prostration increases, the surface temperature falls; and finally the extremities, the face, or the whole body may become cold.

The rectal temperature, however, may remain elevated to the end. The secretions, and especially the urine, become scanty. Albumin and casts are generally present.

In severe cases the patient falls into a condition of collapse, hardly distinguishable from that of true Asiatic cholera. The face is cold and cyanosed, the lips dry, the tongue parched, the breath cold, respirations feeble, the voice suppressed, the pulse weak and thready, and the general condition is one of intense prostration, stupor, or collapse. In mild cases, after a sudden onset and somewhat intense symptoms, the diarrhœic discharges become less severe, the vomiting ceases, fever subsides, and a gradual amelioration of other symptoms occurs. After a day or two practical recovery may ensue. In severe cases the symptoms continue unabated or increase in severity, and finally collapse occurs.

Diagnosis.—The recognition of enteritis offers no great difficulty in most cases. The history, onset, abdominal pain, and diarrhœa are characteristic. When the large bowel is considerably involved it may be difficult to determine whether the enteritis is one of ordinary type or dysenteric. Bacteriological examination of the stools and serum reactions may in these cases be required to establish a correct diagnosis. Sometimes enteritis presents a puzzling resemblance to typhoid fever. The suggestive features in these cases are continued fever, diarrhœa, general prostration, loss of appetite, coated tongue, and headache. The occurrence of splenic enlargement, rose spots, and the characteristic serum reaction eventually establishes the diagnosis in typhoid fever, but a week usually elapses before these occur. Before that time leukocytosis, negative blood culture, general abdominal soreness, and the urgency of the diarrhœa may aid in excluding typhoid fever.

There may be difficulty in distinguishing some cases of enteritis from appendicitis. As a rule, the correct interpretation will be made possible by the persistence and increase of the local signs (tenderness, rigidity, tumor), by the occurrence of repeated nausea and vomiting and perhaps chills, and by increasing leukocytosis. Obstinate constipation, while not necessarily diagnostic, is strongly suggestive of appendicitis.

The diagnosis of cholera nostras usually offers no difficulty whatever. In times of epidemics of Asiatic cholera, however, cases occur in which the diagnosis cannot be made. Under these circumstances no safe rule can be adopted other than to regard all choleraic diarrhœas as of the specific type, particularly as it is well known that mild cases of true Asiatic cholera are frequently seen in epidemics of that disease.

Prognosis.—This is favorable in cases of ordinary enteritis in adults. Unless the cause is one of unusual severity, recovery usually takes place. In the old or enfeebled, however, as in children, the disease is one of considerable gravity. Usually after a few days of urgent symptoms, gradual amelioration takes place, terminating in complete recovery. Sometimes the condition ends in a subacute, or even a chronic disease.

Treatment.—Prophylactic treatment is of the first importance. Among important preventive measures are the avoidance of irritants, tainted food, and the like, especially in hot seasons; in institutions in

which numbers of persons are closely associated, or in camps, barracks, and the like, the closest scrutiny of the food and water supply during the hot seasons of the year is necessary. Careful attention to the dress, especially the wearing of abdominal bands, is of importance in susceptible individuals and is a useful precaution.

The treatment of *acute enteritis* is practically the same as that of ordinary diarrhœa, and therefore needs no extended discussion. The patient should be kept strictly at rest. The temptation to remain out of bed occurs only in mild cases, as the symptoms in severe forms are usually marked enough to make the patient take to bed at once. In the beginning of mild cases, however, matters may be made more serious by any attempt to continue at ordinary occupations, and in severe cases premature release from the bed may cause recurrences. The diet should be restricted to liquids, such as boiled milk, broths, gruels, albumin-water, and the like, or should be interdicted entirely. When vomiting or gastric symptoms are present, it is, as a rule, advisable to withhold all food in the beginning.

Warm applications, such as fomentations, hot-water bags, poultices, or the like, not only give great comfort but have a controlling effect on peristalsis, and thus aid in checking diarrhœa. When distention of the abdomen is troublesome, turpentine stupes may be advantageous.

As soon as the nature of the disease is recognized, the first care must be the removal of irritants from the intestinal tract. Unless diarrhœa is active from the first, a full dose of castor oil or some saline may be used to evacuate the contents of the bowel. If the symptoms in the beginning are not urgent, calomel followed by a saline may be employed. After copious evacuation has been secured, measures should be taken to control the diarrhœa and the intestinal inflammation. Bismuth salts, chalk mixture, lime-water, and other alkalis are advisable when acid fermentation is active. Astringents, such as kino, catechu, or various other tannic acid preparations, may be used. The addition of opium in the form of Dover's powder, laudanum, or paregoric is advisable when diarrhœa is severe and pain is marked. A timely injection of morphine in the beginning may control the severity of the attack. In later stages, when the diarrhœa has become less urgent and the general symptoms are less pronounced, such astringents as silver nitrate or acetate of lead may be used in combination with opium.

In *cholera morbus* the prompt use of opium by mouth or rectum, or of hypodermics of morphine, is advisable. The intensity of the vomiting usually precludes the administration of remedies by the mouth until the condition has been somewhat controlled. After this result has been secured, the treatment may be conducted as in ordinary cases. When symptoms of collapse appear, hot applications over the abdomen are advisable; hot drinks, with the addition of small doses of brandy or whisky, may be given; and hypodermic injections of strychnine, camphorated oil, tincture of digitalis or digitaline, etc., should be employed. When the symptoms have somewhat subsided, great care should be exercised in resuming ordinary diet. Small quantities of liquid food alone should be permitted, and these should be given at short intervals

and cautiously increased. If a tendency to nausea persists, cerium oxalate with fractional doses of cocaine or codeine may be administered before food, so that the stomach may be less irritable.

CHRONIC ENTERITIS

This is a condition of catarrhal inflammation of the small intestine and the upper part of the large intestine, with or without ulceration. It usually follows as the sequel of acute attacks.

Etiology.—This disease may result from a severe attack of acute enteritis or may be caused by repeated slight attacks. Not infrequently it is an accompanient of other conditions of the bowel, as carcinoma, intestinal obstruction, etc. Certain individuals show a distinct tendency to repeated or chronic catarrh of the bowel.

Pathology.—The intestines usually present evidences of long-continued inflammation of the mucous membrane. The surface is covered with excessive secretion (mucous or mucopurulent), and there are areas of thickening of the mucosa or of erosion and atrophy. Ulcerations and stellate cicatrices of healed ulcers may be found, especially in the large bowel. Sometimes polypoid formations are found surrounding ulcers or independent of any ulceration. The mucosa may be of a normal color or hyperemic and more or less pigmented.

Symptoms.—The conspicuous symptom is persistent or intermittent *diarrhœa*. The movements are extremely variable in character, sometimes being nearly normal, at other times soft and pultaceous, or foamy, from the occurrence of fermentative processes. In still other cases they are large and liquid, and their color varies from a light yellow to a dark brown. Frequently they become highly offensive during exacerbations, when increased bacterial putrefaction occurs. In some cases, instead of diarrhœa there is persistent *constipation*. In these cases light-colored or gray scybalous masses, more or less coated with mucus, may be passed; while at intervals attacks of diarrhœa, with soft or liquid movements, occur. When the large intestine is specially involved, mucus is always a pronounced feature in the movements, and at times masses of mucus may be passed without any fecal matter. Blood-streaked movements or decided losses of blood may occur in cases attended with ulcerations or polypoid conditions of the mucosa.

The abdomen is usually distended when chronic enteritis affects a large part of the intestinal tract. In cases in which the process has become limited to a restricted area, distention may be wanting, and local discomfort or tenderness alone may be discovered.

The general state varies greatly. In many individuals this condition persists for years without great impairment of the health. In others, emaciation, general depression, and a variety of nervous symptoms significant of a lowered vitality are met with. Hypochondriac and neurasthenic symptoms are not unusual, as in cases of mucous colitis. The patient may become extremely emaciated, anemic, and weakened, and not rarely sinks into a state of semi-invalidism. The highest grades

of anemia are observed in cases in which ulceration causes loss of blood or in those in which bacterial putrefaction occurs actively.

Diagnosis.—It is difficult to distinguish chronic enteritis from functional disturbances of the intestine on the one hand, and from mucous colitis or certain primary nervous disorders on the other. In enteritis affecting the upper bowel the stools are found to contain undigested food, and are often acid in reaction, as in cases of intestinal indigestion. The intensity of the symptoms and the associated indications of inflammatory trouble alone make a distinction possible. No absolute line of division can be drawn between the two conditions. When the large intestine is specially involved and mucus is abundant in the stools, chronic enteritis closely resembles mucous colitis. The latter, however, is usually so closely associated with primary conditions of nervous debility, and the evidences of intestinal irritation are so inconspicuous as compared with those in enteritis, that a distinction is usually easily made. The history of onset is also of importance in the diagnosis.

Many individuals suffering with nervous diseases, such as neurasthenia, are liable to attacks of diarrhœa, or may suffer with more or less continued looseness of the bowels, which may suggest an intestinal origin for the nervous condition. In these cases, however, acute symptoms of irritation of the bowels are generally wanting and the manifestations are those of intestinal indigestion, rather than of enteritis. When a chronic form of enteritis occurs in tuberculous or syphilitic persons it may be difficult to determine whether it is a simple enteritis or one of specific character. The clinical course and the results of treatment must determine.

Prognosis.—Chronic enteritis may continue for weeks, months, or years. The prognosis is always uncertain but persistent treatment is generally helpful, though not always completely effective.

Treatment.—The removal of all sources of irritation is the first care; sometimes an established error of diet may be discovered and corrected. In other cases a modification of the habits of life and the avoidance of exposure, fatigue, and similar causes are important. A close supervision of the patient's diet and an individual study may discover idiosyncrasies. Sometimes the correction of gastric digestion and the use of remedies such as nux vomica or other stomachics and digestive ferments may relieve the condition. Usually, however, some form of astringent medication is indicated. Of all remedies of this class nitrate of silver is the most important. This may be combined with extract of opium or extract of nux vomica and administered in the form of pills coated with salol or keratin, which secure the passage of the pill through the stomach and its solution in the alkaline secretions of the intestine. Other astringents such as acetate of lead and bismuth salts may be employed. All the remedies are best given in small doses frequently repeated. When fermentative processes are active, guaiacol carbonate or salol may be employed in small doses, as such remedies, by irritating the mucous membrane, may increase bacterial proliferation.

In cases involving the large intestine local treatment is advisable, such as repeated irrigations of the colon with water or saline solution. When

mucus formation is abundant, astringent injections, as solutions of nitrate of silver (1 to 5000), quinine (1 to 5000), or the addition of fluid extract of hamamelis to a saline solution (1 to 125), may be employed.

COLITIS

Inflammation of the colon frequently occurs as an accompaniment of general catarrhal inflammation of the bowels or enteritis and is a common accompaniment of organic diseases of the large bowel. It is also met with as a manifestation of certain specific infections, such as dysentery. Occasionally, however, colitis occurs as an independent disease. This form alone is now under consideration. The term *simple colitis* has been applied to such cases by Hale White.

Etiology.—The causes are similar to those of enteritis, and no adequate explanation can be given for the limitation of the disease to the large bowel. Some cases seem to follow the dislodgment of hardened masses of fecal matter from the sigmoid flexure. Doubtless the retention of scybala in the pouches of the large bowel is quite sufficient to cause inflammation. Dietary errors and various irritants doubtless play a part, and often infections are concerned. No specific microörganism, however, is operative in these cases. Colitis sometimes occurs as a secondary manifestation in certain general infectious diseases, such as pneumonia, septicopyemia, etc., and also in nephritis and uremia.

Pathology.—The mucous membrane of the bowel presents the usual appearances of inflammation with thickening of the mucosa, excessive mucus formation, and follicular ulceration. In persistent cases polypoid formations may be met with, and pigmentation or hemorrhagic extravasation may be seen. In the colitis attending violent infections pseudomembranes are sometimes observed.

Symptoms.—The principal manifestations are diarrhœa, local pain, and tenderness. The stools contain an abundance of mucus, and are often blood-tinged. Sometimes considerable hemorrhage may occur. In severe cases, small mucous, blood-tinged discharges, resembling those of simple dysentery, occur and may be frequently repeated. In subacute cases fecal matter, with mucus and blood, is passed. Abdominal pain, especially in the region of the sigmoid flexure, is usually complained of, and sometimes there is extreme tenderness on pressure. This may be so great that the patient lies with the left thigh flexed; and even the weight of the bedclothes may be intolerable. The pain is increased at the time of the movements, and active tenesmus may occur.

Fever and general prostration of more or less intensity are usually present, and gastric disturbances may occur, although these are not, as a rule, severe. In old and debilitated persons extreme prostration frequently presents itself. In the pseudomembranous colitis accompanying infections a rapid loss of strength, high fever, and prostration result.

Diagnosis.—The acute onset, local tenderness, and mucous discharges are the most characteristic features. It is extremely difficult to distinguish a simple colitis from dysentery or from enterocolitis with special

involvement of the large bowel. It must be remembered that colitis occurs as a symptom of malignant disease and other organic conditions.

Prognosis.—This is usually favorable, although a tendency to chronic inflammation sometimes results. In persons weakened by age or previous disease a fatal termination may occur.

Treatment.—Rest and warm applications to the abdomen, with careful regulation of the diet and the administration of remedies to check intestinal irritation, are the important features. All of these have been considered in the discussion of the treatment of diarrhœa and enteritis. Special mention may, however, be made here of certain local methods of treatment. When the inflammation in the sigmoid flexure and rectum is pronounced, and tenesmus is a troublesome symptom, ice suppositories, injections of small quantities of cold water, or of starch-water containing opium, cocaine, or other sedatives, may be used with advantage. Cases marked by more extensive irritation, or in which hard scybala tend to form, are benefited by repeated injections of small quantities of olive oil. In subacute cases and during the later stages of acute attacks astringents of various sorts may be used in larger colonic irrigations.

DIARRHŒA IN CHILDHOOD

The diarrhœas of infancy and early childhood require special consideration, on account of their greater urgency and their distinctive features. As the digestive and metabolic functions are relatively predominant at this age, any derangement of the gastro-intestinal tract naturally involves a greater disturbance of health.

Etiology.—The causes of diarrhœa in children are practically the same as those in adults, but the difference in the character of the food, in the routine of life, and in susceptibility give a greater prominence to certain conditions.

Food.—Probably the most generally active cause of diarrhœa in children is improper feeding. A mere excess of food may be sufficient to derange digestion and occasion intestinal irritation; but overfeeding is particularly harmful because it furnishes favorable conditions for bacterial growth and fermentative processes in the intestinal tract. This is particularly seen in young children past the nursing age, in whom a single overloading of the stomach may occasion an attack of diarrhœa, afterward prolonged by secondary conditions. The more indigestible the food the more promptly will diarrhœa follow and the more serious its type. In sturdy, bottle-fed infants an appetite somewhat too keen may readily tempt the mother or nurse to overfeed the child, and diarrhœa frequently results. The quality of food, especially milk, must be considered. Diarrhœa in young infants is frequently caused by milk containing too high a percentage of fat.

Much more commonly the cause is some qualitative change in the food, especially the use of tainted milk. Attempts to improve conditions by pasteurization or sterilization of the milk are of questionable utility, although the former plan is preferable. Sterilized milk should be con-

demned, because its constant or repeated use undoubtedly occasions nutritional disturbances, infantile scurvy, and other diseases. Pasteurization, although less objectionable, cannot be relied upon to destroy all microorganisms, and thus often gives a false sense of security. Experimental investigations have shown that after thorough pasteurization bacterial multiplication occurs even more rapidly than in raw milk; and when the food is prepared in the morning, the bottles given later in the day may be in worse condition than if pasteurization had not been practised. The addition of any bactericidal agent to milk, even in minimal quantities, must be unreservedly condemned. Intense forms of diarrhœa and general infection are sometimes followed by the use of milk obtained from cows suffering with mastitis.

Safety in milk feeding lies in the careful supervision of dairies, the handling of the milk in the cleanest possible manner, prompt delivery at the home, and careful refrigeration after its delivery.

Diarrhœas due to milk may be the result of the action of bacteria present in the milk, or may more directly result from poisoning by bacterial products present in the milk. The latter forms are particularly severe and more properly merit the term milk poisoning, which is often used in a general sense to indicate diarrhœal disease due to milk feeding. Investigations have shown the presence of an organism closely allied with the *Bacillus dysenteriæ* of Shiga in cases of infantile summer diarrhœa of the enterocolitis type. There is little doubt that this organism plays an important part in the etiology of some cases and of occasional extensive outbreaks in institutions or in certain communities. It is quite as certain, however, that cases or outbreaks clinically indistinguishable from these are caused by other microörganisms. Among these are various closely allied organisms differing mainly in their capacity to ferment different forms of sugar. Other organisms, however, such as the *Bacillus lactis aërogenes*, the *Bacillus coli* and close allies of this group, streptococci and staphylococci are concerned in some cases. In many cases several forms seem to be associated. The most intense diarrhœas of the cholera infantum type seem to be caused by products of bacterial decomposition either occurring in the food or formed in the intestinal tract. No special microörganisms have been connected with these cases.

In older children various other foods may be the cause of attacks of diarrhœa. Unripe or spoiled fruit, particularly, takes high rank. In certain epidemics it has seemed probable that the source of infection was water. The careless use of impure water in the washing of milk cans or bottles may cause infection of the milk, or the drinking water given the child may cause direct infection.

Age.—The time of greatest susceptibility is from the sixth to the twentieth month, the period of the primary dentition. Dentition itself, by causing reflex disturbances, excessive secretions, or fever, increases the liability to all forms of diarrhœa, although not the direct cause.

Season.—Diarrhœa is distinctly a disease of warm weather, although it may occur at any period of the year. In the summer months it is always more difficult to preserve milk and other foods. In addition,

the children are rendered susceptible by free action of the skin and chilling at night.

Environment.—Surroundings play an important part. Children in crowded cities and amid surroundings of destitution and squalor are much more liable to severe diarrhœas than those in the country or living under more wholesome conditions. In institutions in which a number of children are in close contact direct infections frequently occur. The greatest care is necessary, in the handling of children, to avoid the communication of diarrhœal conditions; particularly should the handling of the diapers be scrutinized with care. Food standing in the same room may easily become infected, and the preparation of the food should be carried out away from any danger of contamination.

Pathology.—The lesions in the various forms of infantile diarrhœa vary considerably; quite commonly the character of the anatomical manifestations is not in keeping with the seriousness of the symptom. Three types may be distinguished, although no sharp dividing line can be drawn between them. These are: (1) simple or dyspeptic diarrhœa; (2) enterocolitis; and (3) choleraic diarrhœa or cholera infantum.

In the first of these the bowel may present no evidences of disease postmortem. When the manifestations have been severe, some indication of catarrhal irritation or inflammation may be found in the upper small intestine and stomach. Congestion, slight thickening, and excessive mucus formation may be discovered. In the enterocolitis of childhood more definite changes in the mucous membrane are seen. Redness and swelling, and frequently enlargement of the lymphatic follicles, are usually met with. Sometimes small follicular ulcerations, and less commonly swelling and slight ulceration of Peyer's patches, may be seen, especially in subacute or chronic cases. In cases of excessive severity pseudomembranes or extensive ulceration may occur, more particularly in the large bowel. After long-continued attacks of enterocolitis, a thinned, atrophic mucous membrane may be found. Various secondary changes in other organs expressive of depletion of the system occur. In cholera infantum evidences of intense inflammations of the mucous membrane, with exfoliation of epithelium and swelling of the glands and lymphatic follicles, may be seen.

Symptoms.—Simple or Dyspeptic Diarrhœa.—Usually evidences of gastric disturbance precede the attack of diarrhœa, and attend it more or less continuously. The child regurgitates food or is attacked by active vomiting. At the same time he becomes restless and distressed, with abdominal pain and distention. The facies and actions suggest griping abdominal pain. Later, diarrhœa sets in, the movements being offensive or sour-smelling, and characteristically containing undigested food, such as curds of milk, together with more or less mucus. The color of the stools varies greatly, sometimes being white or light colored, at other times green. Lesage, in particular, has shown that chromogenic bacteria are active in producing green stools in certain cases. The number of movements may be merely a slight increase over the normal, or may reach ten or more in the twenty-four hours. In some cases the evacuation of the bowels is closely dependent upon the taking of food, one or more

movements quickly following each feeding. In such cases there is apt to be a considerable amount of undigested food in the stools.

The general condition is one of moderate prostration, although frequently there is but little weakness until the diarrhœa has lasted for some time. If long continued, emaciation, pallor, and other signs of depletion are met with.

Enterocolitis.—The term inflammatory diarrhœa is also applied to this variety. The symptoms are distinctly more intense, and in marked cases reach high grades of severity. Nearly always the child loses strength rapidly, and when repeated, and especially watery, stools are discharged, extreme prostration may speedily occur. Fever is practically always noted, and in severe cases is very high. Temperatures ranging from 103° to 105° are not unusual, and hyperpyrexia is a common manifestation of the enterocolitis of the hot summer season.

The *onset* is usually abrupt, and is attended with evidences of general distress, and especially abdominal pain. Vomiting frequently occurs, but is less conspicuous than in the dyspeptic form, and sometimes, especially in older children, may be wanting. Often, however, obstinate vomiting is a marked symptom. The *stools* are numerous, and vary in color from brown to green. After the contents of the bowel have been evacuated, more watery movements, with less and less color, may occur, so that the condition approaches, in the character of the discharges, to the choleraic type. When the large bowel is especially involved, considerable mucus may be mixed with the discharges.

The general condition of the child is one of rapid exhaustion. The face becomes pinched, the eyes grow hollow and are surrounded by circles, the temples are sunken, and when severe exhaustion has developed the hands and feet may grow cold and cyanosed, while the internal temperature as determined in the rectum remains excessively high. The abdomen is often distended and the skin tensely drawn and harsh. The child becomes more and more feeble, its movements less active, its cry more and more faint, and its lips dry. Finally, it sinks into a state of complete collapse. An apathetic, stuporous, or even comatose condition, now and then interrupted by a cry, betokens a condition resembling that of meningitis and designated as spurious hydrocephalus.

In cases involving the large intestine to a considerable degree, violent straining occurs with each evacuation of the bowels, and prolapse of the rectum is not unusual. In all cases the bowel movements may be irritating and cause inflammations of the skin about the anus or buttocks. The urine early becomes scanty, and occasionally the secretion is almost suppressed. Actual nephritis occurs in the intensely infective cases.

When the temperature remains persistently high, various nervous symptoms, such as restlessness, slight twitching, and even convulsions, may occur; but the tendency to prostration usually supplants all other nervous indications, and the child sinks into a condition of lethargy or coma. The loss of flesh and strength sometimes increases with startling rapidity. Complications, such as bronchopneumonia, hyperpyrexia, and extreme nervous symptoms, often precede the fatal termination, but more commonly this results directly from exhaustion.

Diagnosis.—The recognition of this form of diarrhœa offers little difficulty. In the beginning, high fever and the absence of characteristic intestinal manifestations may suggest infectious diseases of various sorts, but usually the characteristic symptoms speedily present themselves. It is practically impossible to separate cases due to ordinary causes from instances of epidermic diarrhœa produced by the *Bacillus dysenteriæ*, except by bacteriological methods.

Prognosis.—Enterocolitis is always a serious disease in childhood, particularly in young infants. Older children more commonly exhibit enough resistance to withstand the attacks.

Choleraic Diarrhœa or Cholera Infantum.—This form, usually met with in early infancy, is of the most extreme gravity. The onset is sudden, and the child becomes prostrated very early. After a few movements, in which the bowel contents are evacuated, a choleraic form of diarrhœa occurs, the stools being large and watery, and containing but little fecal matter. The whole body undergoes a rapid shrinking, and the features present the shrunken, hollow appearance described as occurring in the most violent cases of enterocolitis, but coming on with even greater rapidity. Extreme dryness of the tongue and mouth and excessive thirst are evidences of the desiccation. The urine is scanty or suppressed. The blood becomes inspissated, and the circulation is interfered with, so that cyanosis of the hands and feet, or of the whole surface, becomes marked. The eyes sink in their sockets, the fontanelle is depressed, and within a few hours the child's face assumes the wrinkled appearance of senility. The surface is cold, and stupor or coma develops rapidly. The surface temperature is greatly reduced, while the internal temperature, as observed in the rectum, may rise to 105° F. or more.

The course is brief, and in a large proportion of cases terminates fatally. When improvement occurs there is a subsidence of temperature, a gradual cessation of diarrhœa, and a slow restoration of strength. Not rarely a less degree of diarrhœa persists for some time, due to a residual enterocolitis.

The occurrence of *acidosis* is a grave complication in any of these diarrhœal diseases, and often occurs when there is prolonged inanition or marked dehydration. The alkalinity of the blood is reduced, the urine remaining strongly acid; restlessness and excitement may occur, to be followed by somnolence and finally coma; hyperpnœa is a symptom of grave import. Modern methods of blood examination (CO_2 combining-power, hydrogen-ion concentration) and the presence of ketonuria facilitate the diagnosis.

Prognosis.—The mortality from this form is exceedingly great. When it occurs in institutions, a fatal termination may take place in above 90 per cent. In older children the outlook is less grave, although it is always a condition of extreme severity.

Treatment.—The prophylactic treatment is of the greatest importance. Greater care in the preparation and preservation of food and increased knowledge of the causes of diarrhœa have led to a decided diminution in the frequency of these conditions, although much remains to be accomplished. In hot seasons of the year all forms of food, but par-

ticularly milk, should be kept with the strictest care. When children are bottle-fed, the food if prepared in the morning for the whole day should be kept in a refrigerator. Careful pasteurization is often necessary when the freshness of the milk is doubtful. In the early morning some other form of food, such as barley-water or prepared foods, may be used with advantage until the new supply of the day has been received. In the cases of older children rigid care should be taken to avoid the use of stale foods of all sorts.

The susceptibility of the child may be lessened by the avoidance of exposure. In the summer, when the nights are relatively cool, care in the dress is of importance, particularly the protection of the abdomen and legs. Infectious diarrhœas may be avoided in institutions by the separate management of the children and by the closest care in the handling of the napkins.

Medicinal.—After the onset, treatment should be directed to the removal of irritants, the control of the diarrhœa, and the support of the patient's strength. In the milder dyspeptic diarrhœas the prompt administration of a dose of castor oil and the withdrawal of the accustomed food, substituting for this barley-water, rice-water, albumin-water, weak broths and the like, may speedily terminate the condition. If the tendency to diarrhœa persists, mild astringents, such as powders of bismuth subnitrate, subgallate, or subcarbonate, with or without the addition of pepsin, may be sufficient. More active astringents, like chalk mixture with kino or catechu, and tannic acid preparations of other sorts, may be used. Frequently, small doses of calomel, alternating with bismuth, chalk mixture, or other astringents, appear to have a good effect. When the movements are acid and irritating, alkalis, such as magnesia, soda, or lime-water, may be employed.

In cases of *enterocolitis*, preliminary purgation may be desirable, although it must be used with greater caution than in the dyspeptic diarrhœa, because the tendency to spontaneous evacuation of the irritating matters in the bowel is greater and prostration is more imminent. Sometimes, however, the prompt administration of castor oil or magnesia is desirable. When vomiting is severe, all food should be withheld for a time, or only diluted barley-water, rice-water, or thin gruel given. At the same time, small doses of calomel, alternating with bismuth powder, may be employed. In later stages, astringents, such as have been mentioned before, are useful. Opium in the form of laudanum, Dover's powder, or paregoric is often necessary to check obstinate diarrhœa; and sometimes, when violent purgation threatens speedy collapse, a hypodermic injection of morphine (gr. $\frac{1}{50}$ to gr. $\frac{1}{20}$, gm. 0.0013 to 0.003) may exercise a rapid controlling effect.

When the temperature is high and prostration is severe, colonic irrigations are most serviceable. With the hips elevated, the colon may be flushed without exciting irritation of the bowel, and the effect upon the general condition of the child is frequently surprising. The water used should be of a temperature of from 90° to 80° or 75° F., the amount may vary, according to the age of the child, from half a pint to a quart. A catheter or small-sized rectal tube, passed high into the bowel,

and a fountain syringe, elevated not above a foot or two, suffice for the injections. If the colon and rectum are irritable, the first injection may be at a higher temperature; and a few drops of laudanum may be added to the fluid. Sometimes a small amount of oil or a little starch-water containing laudanum, cocaine or other sedatives, may be injected first. In later stages, if colitis persists and slight diarrhœa with abundant mucus continues, injections of fluid extract of hamamelis in normal saline solution (1 to 65) or nitrate of silver (1 to 8000) may be employed. Stimulants and other supporting measures may be necessary; hypodermics of strychnine (gr. $\frac{1}{400}$ to gr. $\frac{1}{200}$) and small doses of brandy, tincture of digitalis, or tincture of nux vomica may be used. If the external temperature has remained high, sponging or cold packs may be employed with advantage.

In *cholera infantum* the tendency to speedy collapse requires the prompt administration of stimulants. External heat may be needed when the surface temperature sinks. The diarrhœa may be controlled by the use of astringents administered as freely as the condition of the stomach permits. In many cases the prompt administration of a hypodermic injection of morphine will check vomiting and diarrhœa, and permit of the administration of other remedies. When the diarrhœa is under control the cautious increase of nourishment and the use of stimulants are required to restore the patient's strength. The greatest care must be taken to prevent a recurrence of the intestinal disturbance.

The danger of *dehydration* must not be forgotten. Often in these conditions the loss of fluid by vomiting and from the bowel is very great, and must be replaced by fluid administered preferably by hypodermoclysis, intraperitoneally, or intravenously. At times the needles are left in place under the skin and the fluid given by continuous slow drip. If there is no vomiting, water can be given freely by mouth, as the patients are usually very thirsty and will drink greedily. Acidosis must be combatted by the free administration of alkaline solutions (bicarbonate of soda) with or without glucose; if these are given subcutaneously the possibility of sloughing of tissues must be remembered.

Serum treatment has been employed since the discovery of organisms resembling the bacillus of Shiga in cases of infantile diarrhœa, but the results have not proved encouraging.

ULCERATION OF THE BOWEL

A classification of intestinal ulceration is difficult, and from many standpoints unsatisfactory. The most rational is that of Nothnagel:

First Group.—Ulceration as the result of necrotic processes: Simple duodenal ulcer (including peptic ulcer of the jejunum); ulcer following cutaneous burns; embolic and thrombotic ulcer (the peculiar ulcers seen in patients with multiple neuritis belong to this class); amyloid ulcers.

Second Group.—Ulceration as the result of inflammatory processes: Catarrhal ulcer; follicular ulcer; simple ulcerative colitis; stercoral or decubital ulcer.

Third Group.—Ulceration as the result of acute infectious diseases: Typhoid; dysentery; diphtheria; anthrax; sepsis; erysipelas; varioloid.

Fourth Group.—Ulceration as the result of chronic infectious diseases: Tuberculosis; syphilis; erysipelas; leprosy; pellagra.

Fifth Group.—Ulceration as the result of constitutional diseases: Gout; scurvy; leukemia.

Sixth Group.—Toxic forms of ulceration: Uremic ulcer; mercurial ulcer.

Duodenal Ulcer.—The duodenal mucous membrane is frequently the seat of ulceration resembling that found in the stomach. The form under consideration is that which results from digestive action rather than from infectious, toxic, or inflammatory processes.

Etiology.—Duodenal ulcer is found associated with certain diseases, notably of the stomach. As to the association of gastric with duodenal ulceration, according to the Fenwicks, 1.7 per cent. of cases of gastric ulcer were accompanied by a lesion of the duodenum, but Mayo and Moynihan have found that half their cases of duodenal ulcer were associated with gastric ulceration. The clinical history of cases indicates that chronic gastritis with excess of acid secretion is a factor of considerable importance in the development of duodenal ulcer. Nearly all patients give a history of antecedent gastric disorders.

In recent years some surgeons have maintained that chronic appendicitis is a common cause of gastric and duodenal ulceration. The exact mode of operation, however, is uncertain.

Ulcer of the duodenum is more common in men than women and occurs most frequently in the third and fourth decades.

Duodenal ulceration appears to be associated with tuberculosis rather more frequently than it is found in persons free of this disease or suffering with other maladies. Ulceration of the duodenum has also been referred to as occurring in chronic nephritis. These ulcers, however, are somewhat different in their general character from ordinary duodenal ulcers. Extensive burns of the skin are associated with duodenal ulcers, but these differ in character and causation from true duodenal ulcers.

Pathology.—Duodenal ulcers, like those of the stomach, may be distinguished as acute or chronic. The former are circular and punched-out in appearance, and the floor and edges are congested and soft. The chronic or indolent ulcer presents thickened, indurated, and sometimes undermined and irregular edges, and not infrequently has a sloping form, which gives the ulcer a funnel shape. Acute ulcers may be quite superficial, presenting themselves as mere erosions of the mucous membrane. The more chronic forms are deeper, extending to the submucous or even to the muscular coat, and occasionally penetrating through all the coats, when the liver, the head of the pancreas, or some other neighboring structure may form the floor of the ulceration, adhesions having prevented an open rupture into the abdominal cavity. The mucosa surrounding an ulcer, although usually normal, may present evidences of irritative change, and is sometimes irregularly elevated or polypoid. Microscopically the floor and edges of the ulcer present necrotic changes, with some increase in connective tissue, but without the evidences of active inflammatory conditions, such as are found in ordinary ulcerations.

The situation of duodenal ulcers is usually in the first part of the duodenum, near the pylorus. The majority of the ulcers in the first part of the duodenum are situated quite near the pylorus, and are deepest at the upper part where the gastric contents are projected with greatest force against the duodenal wall. The anterior wall of the duodenum seems to be affected more frequently than the posterior, although observers do not agree upon this point.

Secondary Changes.—Duodenal ulcers may undergo a process of gradual cicatrization; but apparently this termination is less common than in gastric ulcers. Chvostek insists that cicatrization is more common than has been generally believed. Perry and Shaw estimate it as occurring in 11 per cent. of all cases. When it occurs there may result a stenosis or deformity of the duodenum similar to the stenoses produced by cicatrizing gastric ulcers. Progressive dilatation of the stomach with symptoms of food stagnation result. Cicatricial stenosis of the lower end of the duodenum or the parts adjacent to the papilla of Vater may occasion obstruction of the biliary and pancreatic ducts. Occasionally diverticula of the duodenum follow the cicatrization of an ulcer. Deep ulcers may cause severe hemorrhage, from involvement of the large arteries adjacent to the duodenal wall.

Perforation of the duodenum occurs in about half the fatal cases. Ulcers upon the anterior wall are more apt to terminate in this way than are those upon the posterior wall, owing to the absence of adhesions. When a perforation takes place without the previous formation of any adhesions the contents of the stomach and duodenum have ready access to the peritoneal cavity, and usually occupy the right side of this sac, extending along the colon toward the pelvis. When adhesions have formed, or when the perforation is minute, a localized abscess may develop. In such cases secondary perforation of the abscess into the liver, the stomach, other portions of the intestines, or the gall-bladder, or through the diaphragm into the pleura, the mediastinum, or the pericardial sac, may occur. In a few instances, rupture into the aorta, portal vein, vena cava, or gall-bladder has been recorded.

Symptoms.—In a large proportion of cases duodenal ulcers are chronic in course and the symptoms are slow in development. Occasionally acute ulceration occurs, and the symptoms make their appearance suddenly, intense pain and acute disturbance of digestion, followed by the rapid development of hemorrhage or perforation, being met with. In the great majority of cases, however, such acute onset is wanting, the symptoms being slow in development and without characteristic significance in the earlier stages. In these cases the patient suffers with gastric manifestations and resulting emaciation, loss of strength and appetite, and finally attacks of pain suggesting hyperacidity. Very commonly the clinical course of duodenal ulcer is characterized by periods of active symptoms followed by remissions, in which complete relief from all discomfort and restoration of strength and normal weight occur. In many instances the condition may be entirely latent until hemorrhage or perforation take place, and cicatrices of old duodenal ulcers may be found at autopsy in cases in which no evidences had

been manifested during life to indicate the disease. The most marked symptoms are pain, dyspeptic manifestations, and hemorrhage.

The *pain* is frequently paroxysmal, like that of gastric ulcer. It may be of intense severity or merely a dull discomfort at certain periods after the ingestion of food. In other cases, whether severe or dull, it is more lasting, and sometimes a constant sense of burning or of sharp pain is experienced. The pain is situated to the right of the middle line, and usually a little above the umbilical level. It may radiate toward the right, or in other cases extend toward the left side. Sometimes it is described as having a deep-seated location, being rather unlike the characteristic pain of gastric ulcer in this particular. The time of its appearance varies. Sometimes it follows immediately after the taking of food, but more commonly it does not occur, or does not reach its acme, until two, three or four hours after meals. The character of the food may have a certain relation to the occurrence and the intensity of the pain. Generally speaking, heavy meals occasion more severe pain; although it may be somewhat later in appearing. The drinking of copious draughts of water or the taking of other liquids, such as milk, beer, wine, etc., may relieve the paroxysm for a time.

Tenderness and rigidity of the abdominal muscles may be met with over the seat of duodenal ulcers, especially those situated anteriorly. Pressure usually increases the pain, although not invariably.

Gastric symptoms are rarely wanting in typical cases. In a great many instances there is a history of long-standing gastric disturbance. The usual symptoms are gaseous distention, acidity, the regurgitation of sour liquid, and especially, dull or sharp pain after the taking of food. Loss of appetite may occur, but more commonly the patient restricts his dietary from the fear of causing pain and other discomfort. In other cases there is an intense craving for food, which is controlled only by the pain that follows its ingestion. Vomiting sometimes occurs. The general condition of the patient is suggestive in the later stages. He is emaciated, sallow, or anemic in appearance, the latter being striking when a slow and continued oozing of blood has occurred; and frequently he presents a desiccated, shrivelled appearance. The bowels are usually constipated, but may be variable, short attacks of diarrhœa alternating with longer periods of constipation. Often constipation is the most marked symptom presented. The stomach contents show hyperacidity and excess of free hydrochloric acid in perhaps one-half of all cases, with normal or moderate acidity in most of the other half. Exceptionally a quite low acidity may be found. The symptoms suggestive of hyperacidity are not always associated with actual excess of acid.

Hemorrhage may occur from the stomach or from the bowel, or the blood may be evacuated in both ways. More frequently there is slight oozing of blood, which may occasion a discoloration of the stools that is just sufficient to be observable; or there may be so little blood that it can be recognized only by chemical tests (occult blood). The continuous presence of small amounts of blood, when associated with suggestive symptoms, is a diagnostic indication of great value.

Perforation of a duodenal ulcer may occasion symptoms similar to those met with in the perforation of gastric ulcers. Usually the onset of this complication is attended with sudden prostration and pain. The patient may sink at once into a condition of shock or collapse; later he may revive and pain in the abdomen, especially toward the right side, tenderness, and distention, due to the development of peritonitis, may then set in. In a great many instances the diagnosis of appendicitis has been made, on account of the acuteness of onset and the tendency to right-sided situation of the symptoms.

Complications.—Among the complications are those which result from extension of the ulcerative process through the duodenal wall, and those which are due to cicatrization of the ulcerated area. In the former group, the most important condition is localized peritonitis. In the case of slowly growing ulcers a certain amount of localized peritonitis, causing adhesion with neighboring organs is frequent. When these adhesions fasten the duodenum firmly to some solid structure and the ulceration penetrates to the serous coat, a localized abscess may occur; or a further penetration into the various structures with which the duodenum has become adherent may take place. When perforation occurs in the absence of adhesions, generalized peritonitis may result; in some instances subdiaphragmatic abscess occurs.

Among the results of cicatrization of the ulcer the most important is partial stenosis of the duodenum, which, in turn, occasions an enlargement of the stomach. Occasionally, when the ulceration has been situated near the papilla of Vater, obstruction of the common bile duct may occasion jaundice or an obstruction of the pancreatic ducts.

Carcinomatous change may take place secondarily and clinical indications of carcinoma may be recognized.

Diagnosis.—A positive diagnosis of duodenal ulcer is frequently impossible. In particular, the distinction from gastric ulcer cannot be made with certainty. This is of minor consequence, as an ulceration just within or just outside the pyloric ring is, to all intents and purposes, of the same consequence. Duodenal ulcer must also be distinguished from gall-stones and occasionally from chronic appendicitis. Reflex hyperacidity and gastritis may simulate ulcer very closely.

The history of long-continued digestive disturbance with occasional remissions is of some importance in the diagnosis. The most suggestive symptoms upon which a diagnosis is usually established are pain and gas, occurring from two to four hours after meals and often at quite a fixed hour in the night, and not rarely yielding temporarily when food or an alkali such as bicarbonate of soda is taken; sour stomach; belching, nausea and later vomiting; constipation.

Fluoroscopic and skiagraphic examinations show active peristalsis with discharge of the bismuth in large masses; peristence of the duodenal cap; later distinct gastric retention. Not rarely, however, the stomach throughout the case shows premature emptying of its contents. In cases of gastric ulcer the symptoms are less remitting, the pain occurs earlier after the taking of food and is often higher up and more superficial; nausea and vomiting are more pronounced, at least in the earlier stages.

Gall-stones frequently occasion gastric symptoms very similar to those of ulcer, but the intensity of pain is greater, its relation to food usually less definite, and the relief from taking food less frequent. Jaundice and tenderness in the right hypochrondriac region are more common. Chronic cholecystitis may lead to the formation of adhesions between the gall-bladder and duodenum, with symptoms scarcely distinguishable from those of duodenal ulcer. Periduodenal adhesions from other causes may result in confusing symptoms, and make a roentgenologic differentiation impossible.

Sudden rupture of a duodenal ulcer, with resulting peritonitis, may be mistaken for appendicitis, intestinal obstruction, acute pancreatitis, and sometimes cholelithiasis. The tendency of the pain and tenderness to extend to the right, and thus suggest appendicitis, should be noted.

The withered, emaciated condition of a patient who has had long-standing ulceration of the duodenum may suggest the existence of carcinoma at the pylorus, particularly when pyloric spasm, constant or paroxysmal, has occasioned enlargement of the stomach and visible peristalsis. There may even be a palpable mass due to periduodenal adhesions and inflammation. In such cases a positive diagnosis is sometimes impossible.

Treatment.—This is practically identical with that of gastric ulcer, which is discussed elsewhere (page 398). As a rule, subacute and chronic ulcers of the duodenum tend to persist, and eventually require surgical treatment. It is wiser to resort to surgical measures as early in such cases as a positive diagnosis is made. When perforation of a duodenal ulcer takes place, immediate surgical operation is imperative.

Duodenal Ulceration Following Extensive Cutaneous Burns.—As yet no satisfactory explanation for the relationship of the two phenomena has been presented. The theory proposed by Hunter assumes that, following the burns, toxic substances are secreted with the bile, which, on coming in contact with the duodenal mucous membrane, induce ulceration. He found substantiation for this view in the experimental occurrence of duodenal ulceration after the subcutaneous injection of toluylendiamin into dogs. However, Fenwick was able to produce the same lesions on repeating the experiment after ligation of the common bile duct. Another view is that the condition is a result of emboli localizing themselves in the duodenal vessels, thus lowering the nutrition of the parts involved and subjecting them to digestion by the gastric juices. Recent studies tend to support this view. Cooke offers the theory that the violent trauma to the skin destroys the antiferments present in the mucous cells, and as the digestive powers of the gastric juice are most potent in the duodenum, digestion of the mucous membrane occurs here. The various theories have recently been reviewed by Novak.[1]

The ulcers differ in many features from the peptic duodenal ulcers. There may be but one ulcer or from three to six present. They are usually located in the inferior horizontal portion of the duodenum. They may be irregular in outline or, as is usually the case, are long and

[1] *Am. Jour. Med. Sci.*, 1925, **169**, 119.

narrow, varying in width from 1 to 5 mm. and in length from 5 to 15 mm. In exceptional cases, ulcers in the stomach or the lower part of the intestinal tract have been found associated with such duodenal ulcers. Usually the ulcer develops from the sixth to the twelfth day after the burn, but they have occurred as early as the second day and as late as the seventeenth. They are met with chiefly in young subjects, rather oftener in females than in males and more frequently after burns of the trunk than on the extremities. They are almost invariably fatal. According to the Fenwicks they occur in 6.2 per cent. of all fatal burns.

Gastro-jejunal Ulcer.—Gastro-jejunal ulcer occurs after gastro-enterostomy for peptic ulcer and is seen, according to Rowlands, after about 1.5 per cent of such operations. It is more frequent after anterior than after posterior gastro-jejunostomy, and may be located entirely in the jejunum near the stoma or along the suture line. Its cause is unknown: various theories ascribe it to operative trauma, the breaking down of hematomas, the presence of unabsorbed sutures, or the flow of hyperacid gastric contents through the stoma. The latter is probably an important factor. The condition occurs more frequently in males than in females; of 31 cases collected by Gorset, 29 were males. The ulcers may be of the acute type, with a tendency to perforation, and with soft walls; or they may be indurated with surrounding adhesions. Peritonitis following perforation is often circumscribed. The symptoms are usually those of the original ulcer—burning or gnawing pain after meals, often relieved by food or alkalies, and at times hematemesis or the passage of blood from the bowel.

Uremic Ulcers.—Difference of opinion prevails as to the probable cause of this ulceration. It has been variously attributed to capillary thromboses, to arteriosclerosis of the intestinal arteries, and to submucous hemorrhages. In all probability the excretion of irritating substances into the intestinal tract is more or less responsible. A feature supporting this view is the fact that in the vast majority of cases of nephritis some degree of catarrhal enteritis is found, undoubtedly caused by the irritation of excretory products; and various degrees of catarrhal and even pseudo-membranous enteritis are usually associated. The ulcers are most frequently found and most numerous in the rectum, colon, and lower ileum, although occasionally they are almost or entirely limited to the duodenum. They vary greatly in size. The smaller ones have regular and somewhat undermined edges. They frequently coalesce, forming large, irregularly outlined areas of ulceration. The condition is usually met with in chronic interstitial rather than in the parenchymatous forms of nephritis.

Embolic and Thrombotic Ulcers.—The intestines are subject to changes dependent upon alterations of the blood supply, just as other tissues. The resulting lesions are dependent not only upon the character of the obstruction but also upon its extent. If a large arterial branch be occluded so as to alter seriously the blood supply of a considerable part of the intestine, phenomena will result, which are discussed elsewhere. If smaller branches be occluded, especially those running in the intestinal wall itself, ulceration will often ensue. Although

thrombosis induced by sclerotic changes in the vessel walls may be the cause of such lesions, a much commoner cause is embolism. The character of the lesion in the intestinal wall will depend upon the character of the embolus, whether it be bland or infectious.

If an embolus occludes one of the smaller branches of an intestinal vessel, a hemorrhagic infiltration of the submucous tissues soon develops and later extends to the mucosa. The area involved becomes swollen, firm, and dark or grayish red. The tissues in the area of distribution of the vessel soon become necrotic, and the mucous membrane with more or less of the underlying tissues is cast off and an ulcer results. Usually the central portion of the area involved shows the most advanced changes. Frequently the visceral peritoneum corresponding to the area of involvement is the seat of a hemorrhagic infiltration. If the entire thickness of the wall is involved, the ulcer becomes much deeper and early perforation may result. Usually the ulcers are small and involve only the mucous membrane and submucosa. They are usually multiple. If the embolus be septic, a localized submucous infiltration of leukocytes occurs and a small abscess forms. This increases in size and finally ruptures into the intestinal lumen. If the involvement of the wall be more extensive, perforation may occur and peritonitis result.

Catarrhal Ulcers.—However inappropriate this term may be, it expresses well enough the nature of the condition—an ulceration occurring in conjunction with and apparently the result of catarrhal inflammation. It is seen especially in catarrhal enteritis of rather long duration, and more frequently in children than in adults. The ulcers are present in both the small and large intestines, but are more numerous in the latter. They are usually minute, round ulcers with very slightly indurated edges. Larger ones may occur which are frequently the result of the confluence of several small ulcers. These larger areas generally have an irregular outline. The ulceration usually involves only the mucous membrane, and at times not even its entire depth. The ulcers are usually numerous, and at times the process is so extensive that only islands of mucous membrane are left between the ulcerated areas. Since the process is limited to the mucous layer, perforation practically never occurs; but it is not unusual to find various degrees of cicatrization when the condition shows a tendency to heal.

The mode of formation of catarrhal ulcers has been the subject of some discussion. The specially mooted question has been whether the primary stage of the process is in the mucosa itself, inducing ulceration by direct action upon the epithelium, or whether there is originally a submucous infiltration inducing ulceration by interference with the nutrition of the overlying parts. Since the catarrhal changes preceding the ulceration are most marked in the mucous layer, and since only the most superficial portions of the mucosa may be ulcerated, the former theory is the more rational.

Follicular Ulceration.—This occurs as a result of the same conditions that induce catarrhal ulceration. In the latter condition the mucous membrane is the portion specially affected, whereas in follicular ulceration the solitary lymphatic follicles are the seat of the process. The

inflammation induces a hyperplasia of the lymphatic elements of the follicles which later undergo central softening. The swelling of the lymphatic follicles interferes with the nutrition of the overlying mucosa and subjects it to mechanical irritation, so that it undergoes necrosis, and the softened elements of the lymphatic follicles escape, leaving an ulcer. As the extent of the follicle is usually greater than the area of superficial ulceration, the resulting ulcer has usually a more or less undermined edge. The ulcers are usually numerous, at times giving a typical honey-comb appearance to the part involved. Perforation seldom occurs. The colon and lower ileum are much more frequently the seat of the process than the upper portion of the intestinal tract, and the condition is more common in children than in adults.

Stercoral or Decubital Ulcers.—These result from the irritant action of inspissated fecal masses on the intestinal wall. This action may be purely mechanical, or, what is more probable, the mechanical injury to the mucosa serves only as the occasion for ingress of pathogenic organisms. The condition naturally is found only in the large intestines, and especially at the points where stagnation occurs, at the hepatic and splenic flexures, in the rectum, sigmoid, cecum, and appendix. The ulcers are usually circular in outline and have an inflamed suppurating base. The condition is more frequently met in elderly individuals subject to constipation. Perforation of a stercoral ulcer has been known to occur. Not infrequently these ulcers lead to cicatrization and stenosis, and probably not infrequently these stenoses have been mistaken for carcinomatous strictures, while Nothnagel calls attention to the possibility of carcinoma developing as a secondary manifestation.

Leukemic Ulcers.—In leukemia, and especially in the more acute forms, it is possible for lymphatic hyperplasia in the intestinal wall to occur, of such a degree as to induce ulceration of the overlying mucous membrane. Such ulcers are more common in the ileum than elsewhere in the intestines, although usually some other portions of the digestive tract, especially the mouth and pharynx, are involved.

Trophic Ulcers.—In various nervous and mental disturbances, ulceration of the intestines has been observed. Extensive intestinal ulcerations have occurred in conjunction with multiple neuritis. In most of these cases sclerotic or thrombotic changes in the vessels were found, so that Nothnagel concluded that the intestinal lesions were the result of the vascular changes associated with the neuritis. Others consider it possible for the intestinal ulceration to result from disease of the brain and spinal cord. In the cases of Targett and Ogle there was fracture of the spine followed shortly by diarrhœa, and at autopsy extensive ulceration of the colon was found. These lesions may be the result of the same factors inducing the superficial trophic ulcerations so common in spinal disease.

Symptoms of Intestinal Ulceration.[1]—There may be a complete absence of symptoms, even in extensive ulceration, especially when the lesions mainly occupy the small intestine. When the colon is involved, and

[1] Duodenal ulcer, tuberculosis, and syphilis, as well as the ulceration of specific infections are excluded.

particularly its lower portions, or the sigmoid and rectum, symptoms are less frequently wanting. Even in these cases, however, there may be a striking absence of clinical manifestations. Among the symptoms, diarrhœa, hemorrhage, or the passage of small amounts of blood, the discharge of pus and shreds of tissue, anemia, pain, fever, and general disturbances of health are the most important.

Diarrhœa is perhaps the most frequent symptom and is caused by the direct irritation of the intestinal nervous mechanism by the ulcerative process or by interference with intestinal absorption. Its character varies with the location of the ulcers. When these are situated in the small bowel, in the cecum, or in the upper portions of the colon, diarrhœa, if present, is of the ordinary kind with more or less fluid or unformed movements. No special characters distinguish the diarrhœa in such cases from that in simple irritation or catarrhal conditions. When the lower part of the large bowel is the seat of the ulcers, there is a greater tendency to admixture of mucus and blood, and the diarrhœa partakes of the nature of dysentery in proportion to the intensity and extent of the ulcerative processes. Intense straining at stool or tenesmus is sometimes met with in such cases, and marked soreness or tenderness over the descending colon or sigmoid flexure may occur.

Hemorrhage is less common than in simple duodenal ulcer and typhoid ulceration. Sometimes, considerable hemorrhage or the passage of blood with each stool may occur, especially when the ulcers are in the lower bowel. Small amounts of blood and occult bleeding are more common. When sloughing attends extensive ulceration, blood, pus, and shreds of tissue may be passed together. Pus and portions of tissue are highly suggestive of ulcerative processes. They are more common in cases of dysentery than in other ulcers, but may occur in any extensive form of ulceration. When intestinal ulceration is attended with large or repeated hemorrhages the patient becomes very anemic. In the early stages, and especially after large hemorrhages, the anemia has the ordinary characters of posthemorrhagic secondary anemia, but in long-continued slight bleeding a more intense anemia results, and often of a type highly suggestive of pernicious anemia.

Pain has no regularity of occurrence. Closely grouped ulcers in the sigmoid or rectum are commonly attended with marked local tenderness and pain of a constant or paroxysmal colicky type. Ulcers elsewhere are less frequently attended with pain, and those in the small intestine rarely cause greater discomfort than occasional attacks of colic or vague soreness. When the ulcers are in the rectum or sigmoid, tenesmus may be pronounced.

Fever is less pronounced than might be expected. In stercoral and catarrhal ulcerations some degree of fever is usual, and at times it becomes marked. In other forms it is not regularly present.

The general condition of the patient is by no means indicative of the presence or degree of ulceration. Sometimes, despite extensive lesions, the patient presents no evidence of great disorder of health. In other cases, especially when diarrhœa, fever, and hemorrhage occur, there may be emaciation, loss of strength, and severe anemia.

Diagnosis.—It is extremely difficult to recognize intestinal ulceration in many cases. The occurrence of diarrhœa, the discharge of blood or pus and blood, and local pain or tenderness are highly suggestive. When ulcers are situated in the rectum or sigmoid region they are readily demonstrable with the enteroscope. Injuries to the ulcerated areas, and even perforation of the bowel, have occurred from the use of this instrument, and it should always be employed with caution.

Prognosis.—Ordinary intestinal ulcers tend to heal in time, provided the proper hygienic, dietary, and medicinal measures are adopted. When extensive ulcers of the large bowel are present there is, however, a likelihood of great obstinacy to treatment. When extreme anemia and emaciation have occurred the prognosis is rather unfavorable.

Treatment.—The treatment of ulcers in the upper part of the intestinal tract does not differ from that of diarrhœa due to other conditions. Careful regulation of diet, rest, local warmth and protection of the abdomen, mild astringents, such as bismuth salts, chalk mixture, vegetable preparations containing tannic acid, nitrate of silver, or salts of lead, are the remedial measures.

Ulcers in the lower bowel can often be treated with advantage by injections or by direct topical applications through an enteroscope. Among the useful forms of injection may be mentioned solutions of nitrate of silver (1 to 5000 to 1 to 1000), weak solutions of salicylic acid, boric acid, thymol, or other antiseptics, astringent lotions, or flushings with simple salt solution. Sometimes nightly injections of olive oil may be advantageous. The regular use of mild laxatives is useful in preventing the formation of scybalous masses.

Direct treatment of the ulcers with stronger solutions of nitrate of silver and other astringents, suspensions of iodoform, and various antiseptics, may prove effective in cases of limited ulceration which can be reached through the enteroscope.

PERICOLITIS

Occasionally inflammation occurs in the tissues surrounding the colon resembling pericecal and peri-appendicular inflammation.

Etiology.—The causes are numerous. Sometimes it results from direct injury; at other times, from organic lesions within the colon or perforation by foreign bodies. Probably in the majority of cases obstinate constipation and stercoral ulceration are the causes of extension and involvement of the tissues surrounding the colon. Various foreign bodies, such as pieces of bone, needles or pins, fragments of straw or wood, and the like, have been discovered penetrating the wall of the colon or lying in an abscess that has formed outside. Attention is called, in the section on Diverticula, to the occurrence of inflammations within and surrounding such extensions from the bowel.

Pathology.—Whatever the original cause, the resulting lesions are similar, although varying in extent. Sometimes there is merely an inflammation or ulceration within and some reactive inflammatory thickening on the outer surface of the bowel. When more extensive

destruction of the mucosa or when complete penetration by a foreign body or perforation has occurred, more extensive external inflammation occurs. This may result in a chronic inflammatory thickening; or, if active infection has occurred, an abscess may follow. Sometimes, such abscesses may discharge into the bowel, and the tumor spontaneously disappears. In many cases the final result of the condition is the formation of fibrous thickenings or of adhesions which may attach the bowel to neighboring structures or cause contraction.

The usual situations in which pericolitis occurs are the hepatic and splenic flexures of the colon or the sigmoid flexure. The term *pericolitis sinistra* has been specially applied to cases occurring in the last-named situation. Perityphlitis of cecal origin is practically identical with this condition; but, because of its close relationship with appendicitis, it is referred to in the discussion of that condition.

Considerable attention has been paid to a form of pericolitis in which the colon is surrounded by a veil-like membrane (Jackson's membrane). Some cases are probably the result of inflammatory conditions; others are probably developmental in origin.

Symptoms.—The clinical manifestations indicate an acute inflammatory trouble with local pain and tenderness on pressure, more or less fever, and disturbance of the function of the bowel. In some cases constipation occurs as the result of inflammatory weakening of the affected segment of bowel or of pressure upon the bowel. In other cases diarrhœa occurs, and sometimes mucus and blood appear in the feces. Sometimes a localized induration or mass may be discovered. In rare instances spontaneous disappearance of the mass may occur in consequence of rupture into the bowel.

Diagnosis.—The condition presents practically the same symptoms as those met with in appendicitis. The location of the lesion usually excludes this condition; but the possibility of a misplaced, and even a left-sided, appendix should be remembered. Some cases in which a tumor has been felt through the abdominal wall have been regarded as cases of carcinoma; and the diagnosis has been disproved only after operation or spontaneous recovery. The acute symptoms and the indications of inflammation and infection should aid in excluding carcinoma, when the possibility of pericolitis is borne in mind.

Treatment.—The treatment of the condition is purely surgical.

APPENDICITIS

Definition.—In a strict sense the term appendicitis should be used to define inflammations of the vermiform appendix. It has, however, obtained a broader clinical significance, embracing various inflammatory affections of the right iliac fossa with which inflammation of the appendix is associated as a more or less important factor. Formerly the term typhlitis was much in use, and was based upon the idea that inflammations of the region designated originated in the cecum and head of the colon and spread from these structures to the surrounding tissues (perityphlitis). In the great majority of instances perityphlitis has its

origin in primary appendicitis, and it may be accepted as established that inflammations around the head of the colon originate in the appendix, and should be dealt with as cases of appendicitis. The term appendicitis is sometimes loosely applied to diseased conditions of the appendix, such as cysts, mucoceles, etc., which are not necessarily inflammatory, although secondary inflammatory conditions may subsequently associate themselves. When used in this way, the term must be recognized as having a clinical rather than a pathological applicability.

Notwithstanding the fact that various surgical writers have denied the existence of primary localized inflammations of the cecum without appendicitis, there is abundant evidence that such a condition does occur. MacWilliams[1] reviewed a number of cases and showed conclusively the existence of both acute and chronic typhlitis independent of appendicitis, tuberculosis, dysentery, cancer, or other like conditions. These forms of typhlitis are due to obscure causes or to coprostasis. The disease of the cecum may go on to ulceration, perforation, and the formation of perityphlitic abscess or general peritonitis, the appendix remaining normal. H. A. Kelly reported 14 such cases. For practical purposes, the comparative rarity of this condition justifies the physician in disregarding it, unless the retention of fecal matter in the cecum is suggested and the signs indicate stasis in that region.

Anatomy.—Embryologically the appendix is a derivative of the cecal pouch, originating as a small process from that structure in the seventh or eighth week of fetal life. In the early stages of the development of the intestinal tube the cecum is situated rather high up, near the under surface of the liver, but subsequently by elongation of the colon it assumes a lower position, carrying with it the developing appendix. Occasionally, the fetal situation of the cecum and appendix is observed in later life. Usually in the adult the appendix lies in the right iliac fossa, its base or point of attachment to the cecum being beneath the point described by McBurney and generally known by his name. This point is situated "exactly between an inch and a half and two inches from the anterior spinous process of the ileum in a straight line drawn from that process to the umbilicus." The attachment of the appendix to the cecum varies considerably. In the majority of cases, or according to Treves, in 90 per cent., a medioposterior position is discovered. Frequently the point of attachment is at the lower portion of the cecum on the anterior or posterior surface, or on the outer or right surface.

The direction is determined not alone by the point of attachment, but also by the length and character of the meso-appendix, as well as by the size and character of the appendix itself. It is of clinical importance that the appendix not rarely occupies a position posterior to the cecum and colon (in the retrocolic fossa) and frequently extends down into the pelvis, and may be attached to pelvic structures.

Meso-appendix.—The mesentery of the appendix is a triangular or quadrilateral fold of the peritoneum arising from the under layer of the mesentery of the ileum and attached by its right border to the cecum

[1] *Annals of Surgery*, June, 1907.

and by its inferior margin to the appendix itself, usually extending about two-thirds the length of that organ from the cecum toward the free tip. The left border of the meso-appendix is free and semilunar or concave in outline. The shape of the mesentery varies to a great extent in different cases, and determines very largely the position of the appendix. Especially important in this direction is the length of its left or free border. The bloodvessels and nerves of the appendix traverse its mesentery, and there may be contained within this structure variable quantities of fat. Occasionally a lymphatic gland (Clado) is found near the root of the meso-appendix.

Considerable variation may be encountered in the shape and position of the meso-appendix, and these variations may determine certain peculiarities in the clinical manifestations of appendicitis. An extension of a serous fold from the appendix to the ovary (appendiculo-ovarian ligament of Clado) is of possible etiological importance. It is supposed to carry bloodvessels and lymphatics, which establish a communication between the circulations of the appendix and ovary. This vascular connection has been denied by some observers (Kelly and Hurdon).

Coats of the Appendix.—These are four in number: (1) The peritoneal or serous; (2) the muscular, including an external longitudinal and an internal circular coat; (3) the submucous; and (4) the mucous.

Circulation.—The arterial supply is derived mostly from the posterior ileocecal artery. The vessels supplying the appendix traverse the meso-appendix, running toward the tip of the organ distributing branches at various intervals. After reaching the appendix, according to Lockwood, they divide into external branches, which supply the serous coat and the muscular tunics, and internal branches which, penetrating the muscular hiatuses, terminate in branches supplying the mucosa and submucosa. The veins accompany the arteries and terminate in the ileocolic and eventually discharge into the superior mesenteric vein, thus communicating with the portal vein. To a slight extent some communication is established with the systemic circulation through the external colic veins.

The *lymphatic* circulation is of great clinical importance. The capillaries begin under the epithelium of the mucosa and beneath the lymphatic follicles, and extending from the submucosa pass through the muscular coats to the peritoneal surface, where they terminate in large trunks accompanying the bloodvessels. They usually extend to the lymphatic glands lying posterior to the cecum, and eventually pass onward to the mesenteric glands along the inner side of the colon. Reference has been made to the small lymphatic gland described by Clado, situated in the base of the meso-appendix close to its attachment with the ileum and cecum. In cases of appendicitis, lymphatic glands in other situations have been sometimes found enlarged, such as those along the external or common iliac vessels, and on this account other lymphatic connections have been assumed to exist. It is not improbable, however, that such enlargements of neighboring lymphatic glands may be the result of diffusion of soluble products of infection, independent of the regular lymphatic channels.

Nerve Supply.—The nerves are derived from the superior mesenteric plexus and terminate in a plexus of Auerbach and a plexus of Meissner comparable to those met with in other portions of the intestinal tract. Through the solar plexus the nervous mechanism of the appendix is connected with the cerebrospinal system and with the right vagus.

Etiology.—Among the causes of appendicitis we may recognize those which are general and those which are determinative. The disease is distinctly one of early life, as is shown by all tables of statistics. The majority of cases occur from the eleventh to the thirtieth year inclusive. Between thirty-one and forty a fair proportion occur, while after forty years the disease rapidly diminishes in frequency, being rarely met with in the aged. It occurs in the first decennium of life in a small number of cases, and has even been recognized as a prenatal disease.

Sex plays a certain part, as the disease occurs in males two or three times more frequently than in females, according to all observers. Some speculation has been indulged in to explain the relatively greater frequency in males, but no satisfactory explanation has been reached. Some authors have believed that the additional blood supply obtained in females through the appendiculo-ovarian ligament prevents obliteration of the circulation, thus obviating an important cause.

Occupation is of no special importance, although it has been claimed that those whose occupation leads to irregularities in eating and to exposure are more liable to the disease than are others.

Nationality probably plays little part. A number of writers have pointed out the infrequency of the disease in the negro.

Heredity is of no special consequence, although families have occasionally been described in which repeated cases have occurred. In this connection the possibility of simulation must be remembered.

Digestive disturbances are perhaps important in a general way, and have often a direct bearing upon the occurrence of the disease. Doubtless chronic gastric disorders may occasion catarrhal conditions of the bowel and favor the development of appendicular infections. A more direct and local relation of gastro-intestinal disease to involvement of the appendix operates in cases in which the cecum becomes distended.

Local Conditions.—Among these, various anatomical conditions require consideration. The appendix normally opens by a relatively narrow mouth, guarded by a reflection of the mucous membrane of the cecum known as the valve of Gerlach. In some instances the valve is wanting or the mouth of the appendix is larger than usual, so that the intestinal contents readily find access to the organ, and may be retained in consequence of narrowing lower down or of weakness in the musculature of the walls. In other instances the mouth, or opening, is contracted, and such contents as gain entrance to the lumen of the appendix in a fluid state may be retained after undergoing inspissation or solidification by the admixture of mucus, epithelial cells, and bacteria, so as to form hardened masses or concretions. In still other cases the arrangement of the meso-appendix or abnormal bands of adhesions that surround the organ at some part of its length, or stenoses and angulations, may similarly prove the cause of retention of material within the lumen.

Sometimes such constricting conditions are so disposed that, while ordinarily of little effect in obstructing the discharge of the contents of the appendix, they may become wholly obstructive when the cecum or other neighboring part of the intestine is distended.

Whatever the cause of the obstruction, the result of retention of material is, according to some authorities, a rapid multiplication of the bacteria contained and possibly, also, an increase in their virulence. This may occasion an infection of the mucous membrane and the subsequent changes described as characteristic of the disease.

There can be little doubt that conditions that obstruct the lumen of the appendix at any part of its course are a frequent and potent cause of inflammation. Not rarely cases are met with in which the distal end, or half, of the appendix alone is involved, while the proximal portion, separated from the former by some obstructing band, angulation, or stenosis, is uninvolved. In some cases repeated attacks of moderate severity occur in which the cause appears to be a temporary increase of angulation and retention of contents, without extensive infection or involvement of the mucosa and other coats. After a repetition of such attacks, a more severe involvement may occur; and the obstructed distal portion may undergo rapid necrosis or gangrene.

Fecal Concretions.—They do not of necessity occasion any inflammatory change, although always a menace, and their relation to appendicitis is, in many cases, a very direct one. Concretions are formed by the inspissation of fecal matter retained in the appendix and by the admixture of mucus, desquamated and exudative cells, and bacteria. According to some investigators, the concretions are always the result of bacterial growth. They are mainly composed of fecal material, with mineral salts, such as phosphate and carbonate of lime and magnesia, and mucus. Such concretions are met with in a relatively large proportion of cases of appendicitis. Deaver found them in about 16 per cent. of his cases; Treves states that they occur in about 30 per cent.; and in other series the proportions have been greater.

Foreign Bodies.—Various bodies, such as pins, small nails, portions of bone, seeds, and fruit pips, as well as other other insoluble substances, may find their way into the appendix, and are occasionally met with in cases of appendicitis. Not rarely parasites have been found, such as *Trichiurus trichiura*, *Oxyuris vermicularis*, and *Ascaris lumbricoides*.

Effects of Concretions and Foreign Bodies.—Although concretions may be met with in appendices that show but little, if any, evidence of inflammatory change, they are a potent cause of inflammatory conditions. In the first place, they are capable, through the pressure exerted upon the mucous membrane, of causing destructive changes in the epithelium, and thus opening the way for the invasion of microörganisms. This is most likely to occur when a concretion has reached a considerable size and when, as the consequence of distention of the cecum or other local conditions, an angulation is produced at the point of lodgment of the concretion. Again, the presence of a concretion may explain the retention of contents within the appendix, and thus may occasion multiplication of bacteria and infection of the mucosa. Frequently when gangrenous

changes occur in the appendix it is found that the lesions have begun at the point of pressure from a concretion; and when perforation takes place the opening is opposite the foreign body. In peri-appendicular abscess, the concretions may be found in the abscess cavity, having escaped from the appendix through a perforation. With respect to foreign bodies of other sorts, it is undoubted that they are capable of exercising irritative and more or less destructive effects upon the mucous membrane and thus of initiating an attack.

Influence of the Lymphoid Tissue.—The lymphoid tissue of the appendix is undoubtedly a factor of importance in the occurrence of the intense inflammation. Not unlikely, the immunity of the aged to the disease is due to the involution that takes place in the lymphoid tissue, and its more or less complete disappearance in later life. No part of the gastro-intestinal tube is so abundantly supplied with lymphoid tissue except the tonsillar region, and it is noteworthy that these two situations are common seats of inflammation in young subjects. It is not improbable that the rich supply of lymphoid tissue occasions a local susceptibility to inflammatory conditions.

Some as yet undiscovered function of the appendix, perhaps of a secretory nature, may play a part in the etiology. Lesions of the colon may be caused by the subcutaneous injection into animals of soluble toxic bodies derived from dysentery bacilli, and it may be that lesions of the appendix may result from the excretion through its mucous membrane of poisons generated by bacterial activity elsewhere.

The Bacteria of Appendicitis.—The microörganisms in cases of appendicitis are varied. By far the most frequent form is the *Bacillus coli*. In many cases it has been found in pure culture but usually some other organism is associated with it. Streptococci or staphylococci may occasionally be found alone but more commonly they are found with other forms. The *Bacillus lactis aërogenes*, the *Bacillus capsulatus aërogenes*, the *Bacillus pyocyaneus*, the influenza bacillus, the bacillus of Friedländer, and a variety of others, have been found alone or in various combinations. In the majority of cases appendicitis probably represents a mixed infection, the most important organisms being the *Bacillus coli*, the *Streptococcus pyogenes*, and the anaërobic forms. Some observations suggest that the milder cases are principally due to colon infection, while the more intense cases are of streptococcic or anaërobic nature.

Pathology.—Various terms have been employed to designate what are sometimes described as different forms of appendicitis, such as simple, catarrhal, perforative, gangrenous, interstitial, obliterative. While these terms are applicable to different stages, they are undesirable if they convey an impression that they refer to different kinds of disease. Unfortunate results have occurred from the impression that mild or moderate symptoms indicated a milder form of disease, such as would be suggested by the terms simple or catarrhal, whereas, in truth, the most serious pathological states of the organ may be present when symptoms have been practically wanting.

The beginning lesion may be assumed to be practically always in the mucosa itself, and in the great majority of all cases there is found

in the appendix removed at operation merely a catarrhal or an ulcerative condition of the mucous membrane. In the least advanced cases slight changes are observed, such as shallow erosion with some accumulation of mucopurulent exudate and congestion of the small vessels in and beneath the mucous membrane. In the more serious grades extensive ulceration of the mucosa will be encountered. At the same time, involvement of the submucosa and of the other tunics may be met with. There may be very pronounced changes in the mucous membrane, with but little visible alteration of the exterior of the organ and but little if any increase in its size. To this form or stage, with its almost exclusive involvement of the mucous membrane, the term *catarrhal* appendicitis is most applicable. Nearly always, however, when the mucosa has been considerably involved, extension to other coats will be found to have taken place. Microscopic examinations show in all stages and grades a tendency to necrosis of the lining epithelium with erosion or ulceration and infiltration of the deeper layers with polymorphonuclear leukocytes. Hyperplasia of the lymph follicles and infiltration with inflammatory cells are regularly present. The lumen of the appendix may become distended with accumulated secretions of a mucopurulent character, and sometimes the exudation becomes hemorrhagic.

In all but the mildest cases the submucosa is involved early; congestion of the vessels and, later, stasis of the blood and thrombosis with œdematous swelling constitute the most conspicuous lesions. In severe cases small or considerable hemorrhages in the submucosa are generally seen. The thrombosis of the vessels may occasion secondary hemorrhagic infarctions of the mucous membrane, and thus advance the process. The swelling and infiltration of the mucous and submucous coats soon occasion a hardening and rigidity of the muscular and serous coats in a direct mechanical way. This is particularly marked when obstructions near the mouth of the organ prevent the discharge of accumulating exudation, and thus occasion distention of the lumen.

Whenever the mucous membrane and submucosa are considerably involved, it is customary to find at least slight disease of the serous membrane. In milder cases a little roughening of the usually smooth and glistening surface is observed, and is found to be due to inflammatory changes in the endothelial cells with beginning fibrinous exudation. The extension of the inflammatory process from the interior of the appendix possibly occurs, as Lockwood has suggested, through the normal gaps in the muscular layer. It thus happens that a considerable degree of peritoneal involvement may occur before the muscular coat is to any great extent involved, except by distention and slight infiltration near the submucous junction. Eventually in many cases the muscularis becomes markedly infiltrated and degenerated, and necrotic changes cause a weakening by destruction of the muscle cells. There is rarely extensive necrosis of the muscularis except when complete occlusion of the circulation through twists, bands, or other forms of obstruction has occurred.

Extensive purulent infection may occasion considerable involvement of the tunics or total gangrene of the organ. In other cases there may

be considerable change in the mucosa and submucosa and considerable involvement of the serous coat, with relatively small grades of destructive change in the muscularis. Infiltration with leukocytes and other evidences of inflammatory change between the muscle cells are more usual.

The *contents of the appendix* increase with more or less rapidity and in varying ways. In some instances, with stricture or other complete obstruction of the outlet, an increasing purulent exudate may accumulate within the lumen and cause distention of the walls, eventually forming a pus-containing sac. More often the amount of exudation is less and there is a tendency to solidification of portions of retained fecal matter with exfoliated epithelium, mucus, and masses of bacteria forming small or large concretions. In many instances there are found within the appendix or within abscesses after perforation hardened fecal concretions evidently of older date.

The effect of increasing accumulation of contents in the lumen upon the walls of the organ is manifested in the obliteration of the folded plicæ of the mucous membrane and the conversion of the lumen from an H-shape to a more or less circular outline. With this stretching of the mucous membrane, there is a flattening of the various structures, follicles, glands, etc., and at the same time a similar effect is produced on the submucosa and outer tunics. In some instances the disease becomes quiescent after this stage.

Obstruction of the lumen of the appendix antedating the attack or the result of inflammatory conditions of its walls has an important etiological relation. Similarly, congenital narrowing of the outlet, acquired changes in the mucous membrane of the cecum involving the mouth of the appendix, or obstructions caused by strictures of the wall of the appendix due to previous attacks or by foreign bodies or fecal accumulations within the lumen play an important part. In all of these conditions retention of the contents may occur, the bacteria multiply and probably gain in virulence, and inflammatory conditions result. In other cases, the mouth of the appendix may be open and its lumen wide enough throughout its entire length to permit of discharge of the contents under ordinary circumstances; but there may be at some point a slight narrowing due to a stricture, a band of adhesion on the outside, a twist or a kink caused by a short mesentery, which may become increased by inflammatory swelling. As a consequence of this increased obstruction the contents are confined to the appendix.

Extensive *necrosis* and *gangrene* may occur very rapidly and sometimes with very slight involvement of surrounding parts. Complete occlusion of the organ at some one point, and especially by anatomical conditions or old adhesions, which exercise a constricting effect both on the organ and circulation, and unusual virulence of the microörganisms concerned in the etiology, may be determining factors. The appendix presents the black or grayish and black appearance of necrosis and gangrene, and hemorrhagic extravasation under the serous coat and more or less fibrinous exudation upon the serosa are observed. The organ is friable and may tear upon the slightest manipulation. In many instances spontaneous rupture occurs.

Involvement of Surrounding Structures.—The most important local result of appendicitis is *peritonitis* involving the folds and fossæ in the immediate vicinity of the appendix. In mild cases and when the infective cause is of a relatively low grade of virulence the serous coat of the appendix is covered with a slight deposit of fibrinous exudation. Such localized peritonitis does not of necessity indicate actual perforation of the organ with escape of infective material, but may occur from invasion of the organisms into the peritoneal coat through the muscular tunics. The peritoneal inflammation may extend to surrounding parts, and a more or less firm agglutination may take place. The process may advance no farther and many cases of appendicitis after reaching this stage subside, leaving behind adhesions to adjacent structures. In more intensely infectious cases the exudation is greater, and localized abscess cavities are formed between the appendix and the neighboring coils of intestine or the abdominal and pelvic walls. Minute perforations of the appendix after the formation of preliminary attachment by fibrinous exudate to adjacent parts hasten the formation of abscesses. On the other hand, a perforation of the organ without preliminary adhesion, and especially a sudden extensive perforation, may be followed by a widespread peritonitis with but little tendency to limitation. Doubtless the virulence and nature of the infective cause play a considerable part in the liability to rapid softening and necrosis of some part of the wall of the appendix, and at the same time determine the amount of fibrinous exudation that may be present. In the more virulent purulent infections, destructive effects upon the tissues are more marked and exudation of fibrin less pronounced.

Peri-appendicular Abscess.—The situation of abscesses resulting from appendicitis varies according to the position of the appendix and of the adjacent parts of the intestine. In the majority of cases the pus cavity is found between the appendix and the ileum at its attachment to the cecum, between the appendix and the head of the cecum, behind the cecum, or between the appendix and head of the cecum and the right abdominal wall and iliac fossa. Less commonly it may be found in the pelvis, in the retrovesical fossa, or in Douglas' pouch. Extension of the infection to the upper part of the abdominal cavity is usually prevented by the omentum and small intestine. In some instances a long appendix lies posterior to the ascending colon and appendicitis may occasion an abscess at some part of its course behind the colon. The wall of the abscess is formed by the adherent appendix, adjacent intestines, other surrounding structures, and by more or less firm masses of fibrinous exudate. The contained pus is usually of ordinary consistence and frequently of fetid odor.

The abscess may rupture in various directions. It may perforate into the cecum or other portions of the intestinal canal, into the general peritoneal cavity, into the pleura, into the bladder or uterus, or through the abdominal wall. In rare instances perforation into the gall-bladder or ureter has been described. After such rupture inspissation of the remaining contents may occur and cure result.

General peritonitis may result from the rupture of a primary abscess, or more immediately from perforation of the appendix in rapid gangrenous or necrotic types of infection. In some cases without perforation of the appendix virulent organisms may escape through the walls of the organ and occasion a general peritonitis, or after the formation of an abscess extension of the infection may occur without discoverable gross rupture of the abscess wall. In these cases of extensive and spreading generalized peritonitis the pus is apt to be thin and serofibrinous from the beginning, and there is but little formation of fibrinous exudate.

Remote Lesions.—Aside from the lesions associated with any form of intense infection, such as myocarditis, infective nephritis, etc., remote lesions may result from invasion of the organisms from the appendix into various surrounding structures. Septic thrombosis of the venules of the appendix is common but fortunately does not frequently extend beyond the smallest branches. In some cases ascending thrombosis takes place and may occasion involvement of the larger mesenteric vessels and the portal vein; secondary pyemic abscesses of the liver result. Extension may take place through the retrocolic veins and sometimes through new-formed collateral branches of the systemic circulation, and occasion secondary abscesses of the lungs.

Chronic Appendicitis.—After a severe attack of appendicitis, or more frequently after repeated attacks, changes may occur in the wall of the appendix and in the surrounding structures which have been described as chronic appendicitis. In a certain measure this term is justified, because the adhesions, distortions, and other conditions met with serve to maintain a state of congestion and lasting catarrhal inflammation of the mucous membrane, and perhaps also a slight chronic inflammation of the outer walls of the appendix. It would be more correct, however, to regard the conditions under consideration ordinarily as results of acute appendicitis rather than as a chronic inflammation in the strict sense. In cases of moderately severe non-perforative appendicitis, with formation of a limited amount of fibrinous exudate, adhesions probably frequently result after the acute inflammation has subsided. Even quite intense inflammations of the appendix and neighboring peritoneal folds may resolve, as is indicated by the discovery in many cases of dense fibrous adhesions that must have followed a previous intense attack of appendicitis with localized peritonitis.

Besides adhesions uniting the appendix to neighboring structures, and which incite to subsequent attacks of appendicitis, the organ itself is frequently found thickened, bent, or otherwise altered by the preceding acute inflammations. Appendicitis of this description furnishes most of the instances of so-called relapsing appendicitis, the thickened sclerotic walls in a measure protecting against perforation and the complications so commonly met with in more acute types.

Obliteration.—This may be the result of previous inflammations, and is thus a form of chronic appendicitis. Some authors insist that obliteration may be purely the result of involution in some instances. In cases of post-inflammatory obliteration, the lumen of the appendix is replaced by a cord of irregularly distributed cells and fibrous connective tissue

surrounded by muscle and a serous outer coat. Sometimes areas of atypical disorganized mucous membrane are found, but in cases of complete occlusion all resemblance to the normal structure is lost.

Symptoms.—In a great majority of the cases of appendicitis the symptoms of onset and the clinical course are more or less similar and distinctive; so that, as a rule, but little doubt exists in the mind of the physician regarding the nature of the disease. A minority furnishes a sufficient number of instances of irregular onset and course to give the impression that the features are quite as often puzzling as otherwise.

In typical instances, pain in the abdomen, diffuse at first, and limited to the right iliac region after a greater or lesser duration; rigidity of the abdominal walls, especially on the right side; nausea and perhaps active emesis; constipation; rigors, or definite chills, accompanied with or followed by fever, acceleration of the pulse, and a general feeling of profound illness, characterize the initial symptoms and the stage of fully developed appendicitis. Wide variations are frequently encountered, and the symptomatology may be said to be as variable as that of any other inflammatory condition affecting the internal structures.

Pain.—Probably the most frequent symptom is pain, which is rarely absent at any stage. It must not be forgotten, however, that even in intense forms, such as those in which necrosis and gangrene occur, pain may be absent from the beginning to the end of the process. Nearly always the patient suffering with appendicitis is seized with a sudden cramp-like abdominal pain, which at first occupies the central or umbilical portion of the abdomen, and subsequently moves toward the region of the right iliac fossa. There are cases in which, from the beginning, whatever pain is encountered is strictly localized in the right iliac region. In other cases the initial pain is vague and difficult to locate.

The nervous mechanism of the appendix explains to some extent the localization of the pain. The afferent nerves are connected with the solar plexus through the superior mesenteric, and thus a connection is established with the splanchnic and the right vagus. The pain of beginning appendicitis is referred to the mid-abdominal region on account of the distribution of the terminals of the splanchnic system to this area. Not rarely, especially in cases in which the appendix has a position posterior to the cecum, pain in the back and in a region posterior to the liver, and even as high as the right shoulder, may be encountered. When the appendix extends downward toward the pelvis, suprapubic, perineal, and ischiorectal pain may be complained of in the beginning, or after a preliminary period of general or mid-abdominal distress.

After the full development of the disease, pain and tenderness, as a rule, are in the right iliac region. There is often a lack of correspondence of the tenderness with the pain. The most extreme tenderness seems to occur in those cases in which the appendix lies relatively near to the anterior abdominal wall, and especially when it is bound by adhesions to the parietal peritoneum. In cases in which the appendix extends downward toward the pelvis and is attached to the bladder or the rectum, or to other pelvic structures, the degree of pain experienced during defecation, micturition, or digital rectal examination may be excessive.

Sometimes the pain is referred to distant parts, such as the thorax, the right thigh, the lumbar region, the back, or the upper portions of the abdomen. The position and attachments of the appendix may, to some extent, determine such referred pains, but this is not invariable.

In the fully developed stage, when pain, previously diffuse, has become localized in the iliac region, the area of involvement is usually limited, and, generally speaking, centres at McBurney's point. The character of the pain varies from a steady ache to a paroxysmal, cramp-like or colic-like condition. Tenderness in the same area is usually, but not necessarily, present.

Cutaneous hyperalgesia appears to occur in nearly all primary attacks at some stage except, perhaps, in the most violent acute forms. The cause of the sensory condition is probably the distention of the appendix. It has frequently been noted that the hyperalgesia suddenly subsides when perforation of the appendix has occurred. In non-perforative cases the symptom gradually disappears. It is frequently present in second or subsequent attacks, but is often absent when the original attack has been sufficiently severe to destroy nervous tissue in the wall of the appendix. The area of hyperalgesia centres about McBurney's point, although it is not strictly confined to this region. More properly it may be said to occupy the region of the eleventh dorsal area of Head, a band extending on the right side from the middle line below the umbilicus to the lumbar spine posteriorly. The hyperalgesia is determined by pinching or stroking the skin, beginning outside the suspected area and working toward it.

Tenderness must be distinguished from pain, although the two usually coincide. The degree of tenderness varies, as has been pointed out, with the character of the case and the location of the appendix. Its intensity varies from the mildest grades, in which it can scarcely be determined, to such severe degrees that the lightest touch or even the weight of the bedclothes is intolerable. In these cases, as in all those in which painful sensations are prominent, the position occupied by the patient in bed is quite distinctive. He lies upon his back or lightly inclined to the right side, and flexes the right thigh upon the body so as to relieve tension upon the affected portion of the abdomen.

Intense pain of a peculiar character is found in those cases of acute appendicitis in which intestinal obstruction has occurred as a complication. The violent pathological peristalsis with tonic contraction of the bowel that occurs in this condition occasions intense paroxysms of pain, recurring from time to time with greater or less frequency. In the beginning these pains may be strictly localized near the seat of obstruction; but later they often become generalized.

Rigidity.—There may be a generalized rigidity in the early stages, when pain also is of a diffuse or generalized character. Later, when the sensory symptoms have localized themselves in the right iliac region, rigidity also becomes limited in its extent and affects the muscles overlying the inflammatory area. A careful comparison of the abdominal walls on the right and left sides will—in most cases of appendicitis, at least—disclose a slight resistance, if not a definite rigidity, affecting

the muscles over the diseased area. The degree of this depends upon the location of the appendix and the character of the surrounding lesions. When the organ lies anteriorly and in close relation with the abdominal wall, and when inflammation involves the structures between the appendix and the abdominal wall, the greatest degree of rigidity as well as of tenderness may be expected. There are, however, instances in which, notwithstanding an immediate relation of a diseased appendix with the abdominal wall, muscular rigidity is totally absent. When the appendix lies posterior to the cecum some spasm of the lumbar group of muscles on the right side may occur.

Reflex Symptoms.—Those affecting the stomach and the bowel are of greatest frequency and significance. Nearly always, in typical cases, nausea occurs. This may be attended with vomiting at the onset, or some time later, and repeated vomiting may take place. Not rarely nausea occurs without vomiting, and may persist until the disease is well developed. Sometimes repeated vomiting may be a very conspicuous feature and may overshadow pain, tenderness, rigidity, and other symptoms usually more distinctive. The character of the vomiting in the early stages is not peculiar. The contents of the stomach are ejected, with perhaps some bile. Intense, uncontrollable vomiting may terminate in stercoraceous discharges; but this is more usually the result of complicating conditions occurring in the later stages.

Constipation is usually a symptom of importance, although not invariably present. In the beginning its cause is found in the reflex nervous influences occasioned by intense pain. Later, inflammatory conditions in the right iliac fossa are mainly operative by causing a local paresis of coils of intestine involved in the inflammatory area, coöperating with nervous inhibition due to pain. In the final stages, when diffuse or generalized peritonitis has occurred, constipation may be the result of a general paralytic condition of the bowels. Various local conditions connected with appendicitis may operate in a purely mechanical way. Thus adhesions between the appendix and the small or large bowel may produce obstruction; or large abscesses may compress and practically obliterate the lumen of the bowel. In some instances there is at first no disturbance in the action of the bowel, one or more normal movements occurring after the onset. In some cases a diarrhœal condition may exist for a time, but such cases are rare.

Symptoms of Infection.—These usually occur, although there are cases in which, despite the existence of a definite infective lesion, generalized symptoms fail to make their appearance. Rigors and chills occur at the onset of many cases. Sometimes these are pronounced and repeated.

Fever usually appears, although it must be recognized as a symptom of uncertain value. In many cases, in spite of the seriousness of the local lesions, the temperature remains low, while in other conditions simulating this disease fever is of at least as great frequency as in ordinary attacks of appendicitis. In the average cases the temperature soon rises after the onset, being as high as 100° to 102° F. within a few hours. Subsequently, a variable temperature is apt to mark the course. Often the temperature falls to the normal soon after the onset, without refer-

ence to the character of the local lesions. Sometimes a continued fever may be present for several days, and may terminate in an irregular fever when peri-appendicular inflammation or abscess has developed. In most instances fever is an uncertain indication; the severest forms of appendicitis may be unaccompanied by elevation of temperature.

Occasionally subnormal temperatures are encountered, and are usually significant of rather intense infections. On the other hand, extremely high temperatures may occur in severe infections with marked local reaction. Even extensive peritonitis may be unattended with elevated temperature. In the later stages, when localized abscesses have formed, irregular fever is usual but not invariable.

The *pulse* indicates the general condition of infection with somewhat more reliability than does the temperature. In many cases in which fever has been absent, rapidity of the pulse has, from the beginning, indicated the existence of a serious lesion. The character of the pulse varies with the nature of the infection and the local conditions. Acute inflammatory lesions with marked reaction are usually attended with a rapid but relatively full and tense pulse. On the other hand, infections extending to the peritoneum, and especially diffuse peritoneal involvements, are accompanied by increasing rapidity of the pulse, often with irregularity and loss of quality. Less intense peritoneal involvement sometimes affects the quality of the pulse in a different manner. In such cases a hard or wiry pulse of moderate rapidity and without any irregularity may be met with. Increasing rapidity of the pulse, loss of quality, and the occurrence of irregularity are grave indications.

Chills sometimes occur at the onset or throughout the course. A considerable proportion of cases begin with rigors or a sense of general coldness, after which nausea and the other symptoms set in. The chills usually cease after the disease is fairly established, and there is no tendency to recurrence until extension of the infective process has caused peritonitis. In peri-appendicular abscess, recurrent chills may continue for a long time. Still more marked is the tendency to chills accompanying widespread infection, as in pylephlebitis.

Leukocytosis.—The condition of the blood is usually significant of an infective inflammatory lesion. In the great majority of the cases of appendicitis there is a definite leukocytosis, the number of leukocytes usually exceeding 12,000 to 15,000 per cmm. The differential count shows a marked preponderance of the polymorphonuclear elements, sometimes reaching extreme grades, such as 90 to 95 per cent. When localized peritonitis has developed, the leukocytosis may be increased to greater figures; but a spreading peritonitis with intense general infection is apt to declare itself by a falling leukocyte count after a preliminary leukocytosis. A leukocytosis is not, however, invariably present and even in cases of abscess formation the leukocyte count may be normal or subnormal but such cases are rare. Some maintain that a preponderance of polymorphonuclear elements without an actual numerical leukocytosis may occur in appendicitis, but this is rare and its significance may be questioned.

Physical Signs.—Among the objective manifestations of appendicitis those which attend the earliest stages are of the greatest importance, as prompt diagnosis is most essential to proper treatment. Rigidity is undoubtedly a sign of extreme value. Somewhat later than this other objective evidences may be found, among which tumor and abdominal distention are most significant.

Tumor.—At the time of the primary rigidity a certain fulness in the right iliac fossa is usually detected. In part, this is the result of the rigid condition of the rectus muscle, which opposes a resistance to the palpating hand and gives the impression of a mass. If the tenderness is not too great, this rigidity may be overcome and the suggestion of a mass disappears. Very frequently, however, there will be found below the rectus muscle a rounded and somewhat yielding tumor-like resistance, caused by gaseous distention of the caput coli. The nature of this mass may usually be detected by percussion over it, when tympany shows that it is air-containing. The percussion note is not so purely tympanitic as that on the opposite side, probably on account of the thickening by congestion of the surrounding bowel walls and perhaps also the rigidity of the abdominal muscles.

In the later stages, when a peri-appendicular abscess has formed, this may be readily detected as a more or less resilient swelling, or sometimes as a firm mass, without any discoverable indication of fluctuation; but the character of the tumor differs mainly in consequence of its varying situation. When placed anteriorly to the appendix and cecum, extreme tenderness to touch usually renders palpation more difficult and uncertain in its results; but, at the same time, more frequently enables the examiner to determine the existence of fluctuation, as well as the suggestive dusky discoloration of the skin and the subcutaneous œdema. Abscesses on the inner side and posterior to the cecum and appendix cannot be felt so readily, usually cause less superficial tenderness, and are more likely to give the impression of considerable hardness. Not rarely it is difficult to distinguish such from solid growths by palpation alone. Abscesses extending downward toward the pelvis may be so deeply situated as to escape detection through the abdominal wall, but may be felt, upon vaginal or rectal examination, as resistant, elastic, or boggy swellings. The size of peri-appendicular abscesses varies greatly, the majority not exceeding the size of an orange before rupture takes place. Sometimes, however, masses considerably greater than this are encountered, and may by their very magnitude prove deceptive. When external pointing takes place, the appearances are those usual in deep-seated collections of pus that have reached the surface.

The Appendix May Sometimes be Palpable.—Some authors have claimed that this is frequently the case. Most writers, however, agree that a positive recognition of the enlarged or diseased appendix is seldom possible. In exceptional cases it is exceedingly easy to feel some portion of the appendix or a large part of it. It is not difficult to be deceived and to mistake inflammatory exudates, distended coils of intestine, etc., for the appendix itself. Occasionally, when the appendix is attached to the anterior abdominal wall, the attached

portion may be felt as a mass that seems surprisingly near the surface. In other cases the tip of the appendix has been felt high up on the right side of the rectum. More commonly masses here palpated are peri-appendiceal abscesses.

Abdominal Distention.—Distention of the intestines is usually an early sign, and sometimes increases with great rapidity. The caput coli is often slightly dilated in the beginning. At the same time, slight general meteorism may be observed. In later stages, increasing distention may take place from one of several causes. If the appendix is ruptured, or if an extension of the infection has occurred through the wall of the unruptured appendix, the result is peritonitis with more or less rapidly increasing tympany. In other cases the distention is the result of obstruction of the lower portion of the ileum, in consequence of violent local inflammation or of ileus resulting from obstruction. Rapidly increasing general distention occurs as in other forms of acute obstruction. The absence of distention by no means excludes extensive local inflammation; and even with peritonitis the abdomen may remain comparatively flat.

Vesical Symptoms.—These are frequent. In the beginning there may be pain in the region of the bladder or retention of urine, as the result of nervous reflexes caused by the acuteness of the pain; and retention may persist throughout the whole course of acute cases. As a rule this disappears after the first day. Subsequently, and at times from the beginning, there is, on the contrary, a continuous desire for micturition, especially when the appendix extends downward toward the pelvis, and pericystitis is present. In such instances the vesical symptoms may dominate the clinical picture. Actual cystitis may develop from direct extension or in consequence of general infection.

The urine frequently presents small quantities of albumin, with a moderate number of hyaline or granular casts. In some instances of greater severity a well-defined infectious nephritis may occur, especially in cases of extensive abscess formation. Albumosuria is of no regularity of occurrence and of no diagnostic value. In rare instances peri-appendicular abscesses have ruptured into the bladder or ureters.

General Peritonitis.—This is the most ominous of the results of acute appendicitis. Unfortunately, this condition may develop very promptly in patients who have presented no symptoms of great gravity; and it is equally unfortunate that it may arise in the late stages after a somewhat benign course. In a small proportion the disease apparently begins with general peritonitis. The onset is usually marked by somewhat abrupt indications, significant of rupture of the diseased appendix or of extension of infection to the peritoneum. Sharp pain or suddenly increased local tenderness and rigidity, rigors or chills, a rapidly increasing acceleration of the pulse and elevation of temperature, or, in cases of marked infection, a fall of temperature with prostration and symptoms significant of shock, are mostly those which indicate the beginning of this grave condition. Soon board-like rigidity of the abdominal muscles, intense tenderness or hyperesthesia over the affected area, sometimes involving the whole abdominal wall, an anxious expression, a hard, small pulse with increasing rapidity, and a dorsal decubitus with a tendency

to flexion of the right thigh, are significant of its extension. Still later, the acute symptoms may ameliorate with advancing infection and overwhelming toxemia. At the same time increasing abdominal distention takes place, and the patient presents the facial and general appearance of one profoundly septic and having spreading abdominal disease. Vomiting may mark the onset, and may continue until extreme prostration from septicemia puts an end to this as well as to other acute symptoms.

Septicemia.—General septic infection may occur with or without extensive local lesions. As a rule it is most marked in those cases in which the local infective lesion is decided. Irregular chills and high and irregular fever, with a rapid, weak pulse and a tendency to drenching sweats, indicate this complication. Septic symptoms are most marked in those cases in which infective thrombosis extends from the diseased area through the mesenteric into the portal veins, establishing a suppurative pylephlebitis. In these cases, in addition to the evidences of a general septic process, pain is met with in the region of the liver; swelling of the liver may be detected, and jaundice appears. The last-named symptom may occur without pylephlebitis or pyemic abscess, as the consequence of an intense septic infection, but is rarely marked in such instances. Pyemic abscesses in other organs, as the lungs, spleen, and kidneys, acute swelling of the parotid gland, and acute infectious nephritis, occasionally occur. Subphrenic abscesses have been encountered in some cases, mainly as a result of extension of cellulitis behind the cecum and colon. Pleurisy may follow or occur independently.

Clinical Varieties.—The nature of the process is not essentially different in mild and severe cases, and such terms as "simple appendicitis," "simple catarrhal appendicitis," "gangrenous appendicitis," and the like, are in a certain sense mischievous if they create an impression that there are forms of appendicitis of essentially different character, and that mild symptoms point to the existence of a benign process, while severe symptoms indicate more serious disease. The mildest of symptoms may be encountered in cases in which extensive necrosis or gangrene has occurred, while severe symptoms may be met with in cases in which a relatively slight disease of the appendix exists. It cannot be denied that there are many instances of appendicitis in which the mucosa is involved to the practical exclusion of the other parts of the organ. Such cases are, properly speaking, catarrhal appendicitis. Doubtless many such cases occur without clinical symptoms of any sort, in proof of which the experience of the postmortem table might be cited. A second group of cases is that in which all the walls of the appendix are involved, with little or no extension outside; cases in which the disease is confined to the appendix itself. In a third group the disease has extended beyond the appendix and involved the peritoneum or other structures. Finally, there are cases in which a general peritonitis is associated.

The infective agent may be the same in all of these forms, and the pathological changes do not differ in kind. The different clinical and pathological course is dependent upon varying local conditions affecting the circulation in the appendix and its drainage, and perhaps upon anatomical conditions promoting in some and preventing in other cases rapid extension of the infective process.

Lesions Limited to the Interior of the Appendix.—There are cases of simple catarrhal appendicitis in which sudden abdominal pain, at first somewhat general, later limited to the right iliac fossa, slight tenderness and rigidity in the same regions, chilliness followed by slight fever and acceleration of the pulse, a little nausea and perhaps an attack of vomiting and constipation, make up the clinical picture. Sometimes, indeed, little beyond pain and tenderness occurs. After a variable period extending from a few hours to twenty-four or thirty-six hours the symptoms subside, leaving a variable degree of soreness that may persist for several days longer. The subsidence of symptoms is often coincident with evacuation of the bowels. Many such cases are instances of merely catarrhal inflammation, and the pathological lesions are often confined to the mucosa or mucosa and submucosa.

Formerly cases of this sort, in which sudden abdominal pain and tenderness are the principal symptoms, were described by some as cases of "appendicular colic," especially when fever and other manifest indications of inflammation were wanting. There seems little reason for believing that these cases are other than actual appendicitis, and even the possibility of a colic of this description arising in an uninflamed appendix must be doubted. Nor is it certain that the colicky pains of actual appendicitis are even due in large measure to peristalsis of the muscular layers of the appendix.

Unfortunately, the pathological conditions are not always as limited as have been described in cases presenting the symptoms indicated. There may be, with symptoms no more intense than these and with no greater duration so far as can be discovered, extensive necrosis or gangrene of the appendix and the presence of fecal concretions. Indeed, appendicitis of the greatest gravity may be entirely latent, the first symptom appearing when perforation and peritonitis have occurred.

Involvement of the Whole Thickness of the Organ.—In cases in which a rapid extension of infection causes almost immediate involvement of the entire wall of the appendix the symptoms are usually more intense, the initial rigor or nausea more pronounced, the fever higher, the local symptoms more pronounced, and, in general, the patient's condition seems more serious. If subsidence of the symptoms occurs, this is more gradual and the local tenderness and rigidity are more prolonged. In the simpler cases there is often a temporary amelioration of symptoms after free evacuation of the bowels, even though the purgation has no permanent good effect. Such relief is much less likely in the cases of extensive involvement of the walls than in cases of the catarrhal type. Associated involvement of the serous covering adds to the gravity, and in a considerable proportion is followed by a localized peritonitis.

Involvement of Surrounding Structures.—In some instances, after an acute onset, moderate symptoms may continue for a period of from one to three or even five days, when an exacerbation sets in and evidences of extension of the infection present themselves. In these cases the local symptoms, as well as the fever, nausea, and vomiting, subside, and a few evacuations of the bowels may add to the apparent improvement. Gradually, however, or sometimes quite suddenly, a renewed chill or

vomiting and the reappearance of sharp pain initiate the extension to the peri-appendicular structures. Such cases are probably in most instances caused by organisms of relatively low virulence, and occur in individuals whose general or local conditions offer considerable resistance. Unfortunately, however, the sequence of events is often far from being as satisfactory as this. In many instances there is a rapid extension with constantly increasing symptoms, and considerable localized peritonitis develops before any adequate amount of exudate can form to limit the spread of the infection by causing adhesions. After spreading to a certain distance, however, further extension may be prevented by exudation and agglutination of the bowels. In this manner general peritonitis may be prevented, and eventually a peri-appendicular abscess of considerable size may be formed. The symptoms significant of such extensions are usually quite marked, consisting of increasing local tenderness, rigidity, and swelling, increased but often irregular fever, general meteorism with obstinate constipation, indications of cessation of local peristalsis, and finally increased vomiting, perhaps becoming stercoraceous in character.

In many cases the involvement of surrounding structures occurs suddenly after perforation of the wall of the appendix. Time of rupture may be indicated by an attack of renewed and severe pain, by a sudden feeling of sinking or prostration, nausea or vomiting, or fall of temperature and acceleration and arrhythmia of the pulse. In other cases no special symptoms occur, but the general features take on an aspect of greater gravity and the local symptoms become more marked. Soon the indications of a circumscribed or general peritonitis appear.

Chronic Appendicitis.—Two types may be recognized. The first is one in which, as the result of a previous acute attack, general thickening of the walls of the appendix has remained, or a narrowing of the outlet, an angulation, or some other condition interfering with proper drainage. In these cases local or general abdominal symptoms may be more or less continuously present. In the second group, as a result of shortening or abnormal attachments of the meso-appendix, or in consequence of angulations or adhesions, the appendix, although ordinarily free from inflammatory conditions, is prone from time to time to suffer when sluggishness of the bowels, gaseous distention of the cecum, and especially fecal accumulations in the caput coli or cecum occasion increased tension upon the appendix, increased angulation, etc. Under these abnormal conditions frequent mild acute attacks may occur, and may be quickly relieved by free evacuation of the bowel or correction of the other conditions named. With each recurring attack, however, the appendix tends to become more distorted and damaged, and eventually a violent acute attack may terminate the condition with all the manifestations of a severe acute appendicitis. It is this form to which the term *relapsing appendicitis* has been particularly applied. While this name is used especially to designate cases in which acute appendicitis is supposed to occur from time to time in a relapsing manner, and without any special local condition persisting between the attacks, it is important to recognize that the type above described is probably equally common,

or more common, namely, that in which recurring attacks of increased tension or angulation take place without necessarily marked inflammatory conditions, until more severe lesions are finally established.

In chronic appendicitis of the first type, due to general thickening, adhesions, etc., persistent local soreness, increased from time to time when distention of the bowels occurs, a tendency to more or less troublesome constipation, sometimes an associated mucous or membranous colitis, and evidences of intestinal indigestion, with furred tongue, disturbed appetite, nausea, tympanitic distention, and vague generalized abdominal pains, are met with. Not infrequently attacks of severe cramps or colic may occur when the intestines are particularly sluggish.

In the *relapsing type* attacks occur indistinguishable from those of acute appendicitis, arising without any previous history of involvement of this region. In other cases there are, occasionally, short seizures in which intense localized pain and tenderness, with perhaps slight muscular rigidity, make their appearance without much fever, disturbance of the pulse, or constitutional disorder. When the attacks subside, the return to normal conditions is often so rapid that the thought of a severe local inflammation can hardly be entertained; and an examination of the blood in these cases usually reveals but little, if any, leukocytosis. It is frequently observed that the acute attack follows some very definite derangement of digestion; and the association of the latter, with the consequent localization of symptoms in the epigastrium or upper portions of the abdomen, and the presence of symptoms suggesting "biliousness," may readily lead to an overlooking of the appendicular disease.

The outcome of chronic appendicitis may be the development of a chronic intestinal disorder, such as membranous or mucous colitis or habitual constipation. In cases of the recurrent type there may be a subsidence of the attacks after several have occurred, and even after attacks of intense violence. There is always, however, the danger that finally a very severe condition may develop; perforation or extension of inflammation to the peritoneum may occur; and the disease may terminate as do instances of violent primary appendicitis.

Diagnosis.—The symptoms of acute appendicitis, when marked, are usually so typical that the diagnosis can scarcely be mistaken. There are, however, many instances of obscure and even of latent appendicitis, in which no amount of clinical acumen or painstaking care will enable the practitioner to determine correctly the disease, although suspicion may attach to the appendix. On the other hand there is unfortunately a tendency to regard every form of abdominal pain as appendicitis, unless the evidence clearly points to some other disease. However common appendicitis is and however important its early recognition, it would be a misfortune if physicians generally disregarded all that has been learned respecting the diagnosis of this disease to such an extent as to suspect its presence in all cases of abdominal pain, unless clear evidence of something else were at hand.

The development of sudden pain in the abdomen, followed by a localization in the right iliac region, and attended with rigidity of the muscles over this part, must be looked upon as having great significance.

If, in addition, there has been a primary rigor, or nausea and vomiting, with constipation, the diagnosis becomes fairly assured. Fever is a symptom of little importance, and rapidity of the pulse, although a little more trustworthy as an indication, is not necessarily met with. When the pain becomes sharply localized in McBurney's point, and muscular rigidity is found in the same area, the diagnosis is practically established. The existence of leukocytosis is often an aid in differentiating between appendicitis and other affections in the same region.

The Diagnosis of the Character and Stage of the Disease – It is often impossible to distinguish between mild appendicular lesions limited to the inner lining or to the walls of the appendix alone and cases of a severer grade, with beginning or even extensive peri-appendicitis. In many instances, however, a diagnosis of the grade of the disease is possible. Simple catarrhal appendicitis is usually recognized by the mildness of the symptoms, by the tendency to rapid amelioration after evacuation of the bowel, and by the early return to normal condition. In cases, however, in which the symptoms are of equal moderateness, but tend to persist in spite of movement of the bowels, and in which even slight tenderness and fever persist, the probability of a more serious condition must be considered. When the severity of the constitutional condition is distinctly out of proportion to the local manifestations, this may properly be suspected of being due to a more intense, and perhaps necrotic or gangrenous, lesion. Marked leukocytosis is an additional indication of severity and of probable peritonitis.

Peri-appendicular infection and the development of abscess may be indicated by the continuous increase of local symptoms and the appearance of tumefaction in the right iliac fossa; or by the recurrence of fever, pain, and rigidity after an interval of quiescence succeeding the initial attack. Sometimes the development of peri-appendicular abscess is so gradual and insidious, and the exudative material and agglutinated coils of intestine so thoroughly walled around the focus of disease, that an abscess of considerable size may develop with relatively no local symptoms; and there may be but little fever and other constitutional reaction. In such instances, leukocytosis may be wanting, even though an abscess of considerable dimensions has formed.

Extensions of the infective inflammation to neighboring veins or lymph channels, causing an ascending suppurative phlebitis of the mesenteric veins, and finally of the portal vein, or a lymphangitis of the retrocecal region, are indicated by evidences of intense toxemia and septicemia and by localized symptoms of marked gravity. In the case of retrocecal inflammation the pain may be confined to the back, and may extend upward toward the posterior aspect of the liver.

The development of a spreading peritonitis is indicated by intense constitutional disturbance. The general appearance of the patient is usually somewhat significant. Increasing local tenderness and swelling, with recurring rigors and elevation of the temperature, and with marked disturbance of the pulse rate, followed by general abdominal distention and a cessation of peristalsis, are among the important indications. Leukocytosis may at first rise to higher levels; but in many instances,

especially those of severe infectiousness, the leukocyte count suffers an early fall. This may set in so promptly that, by the time the first examination of the blood can be made, a normal count, or even leukopenia, may be discovered.

Differential Diagnosis.—The onset must be distinguished from that of a variety of abdominal conditions, any one of which may bear so puzzling a resemblance as to make a certain diagnosis impossible.

Painful gastro-intestinal conditions of various sorts must be distinguished. An attack of simple gastric indigestion or of acute gastritis frequently begins with symptoms like those of appendicitis. As a rule the relation to some indiscretion of diet is more immediate and certain; the localization of the pain is more likely to be in the region of the stomach, and to remain in that place; nausea and vomiting and tenderness in the epigastrium are conspicuous; while fever and leukocytosis are less likely to be found. The latter symptoms, however, may occur, especially in children, and the local symptoms may be referred to lower parts of the abdomen, particularly when the gastric disturbance has been occasioned by a sluggish condition of the bowels.

Acute, painful affections of the small intestine more frequently bear a striking resemblance, and usually in proportion to the nearness of the approach of the irritative or inflammatory conditions of the lower part of the small intestine. Usually the pain and tenderness are more diffuse, and throughout the attack fail to become limited to the right iliac fossa. Rigidity is more general, when present; and the pains are of a more distinctly generalized colic-like character. Disturbance of the stomach is less marked, and diarrhœa more likely to occur. The condition is less liable to present the rapid development of grave symptoms met with in severe cases of appendicitis, and is less likely to undergo the amelioration after free purgation seen in the mild cases of appendicitis.

Intestinal *colic*, whether due to digestive disturbances or to inflammatory conditions of the intestines, may suggest appendicitis. (See Acute Enteritis.) The resemblance of lead colic is often striking, on account of the association of obstinate constipation with the acute abdominal pain. The indications of localized inflammation, however, are wanting, other signs of plumbism are usually present, and a careful scrutiny of the history and a consideration of the occupation usually prevent error.

Acute *enteritis* due to mineral poisoning, such as mercury, or arsenic, as well as attacks of food poisoning, may simulate appendicitis. They are distinguished by the general extensiveness of the abdominal symptoms, the absence of localized tenderness or rigidity, and the prostration. Usually there is more or less, and sometimes intense, diarrhœa.

Acute *colitis* resulting from stagnation of the contents of the large intestine and the accumulation of fecal masses in the cecum, or following exposure to cold or digestive disturbances, may simulate an attack of appendicitis. This is particularly the case when the cecum or the head of the colon is especially involved. In some instances an accurate diagnosis is impossible; and it is certain that in some of the cases the appendix becomes secondarily involved, when it must be obvious that

the symptoms would be even more puzzling. Attacks of typhlitis due to stercoral accumulations usually present a less intense degree of local tenderness and rigidity, and are less acute in onset than appendicitis; but cases have been reported in which the local conditions have been violent, and in which stercoral ulcerations have caused perforation with the secondary development of perityphlitis.

Typhoid Fever.—The intestinal conditions in the early stages of typhoid fever may simulate appendicitis. Rigidity of the abdominal walls, marked local tenderness, and tumefaction occur in these cases; while fever and the general constitutional symptoms of the onset resemble those of many cases of appendicitis. The gradual onset after a week or more of indefinite malaise and gradually increasing fever, the complete anorexia, the dilated pupil, and the absence of leukocytosis, may aid in the recognition. Unfortunately, some instances of typhoid fever with the particular localization of the lesions referred to, come on very abruptly, with marked symptoms resembling those of appendicitis. To add to the confusion, there is, in a certain number of cases of typhoid fever, an early involvement of the appendix, with the development of specific typhoid lesions in the lymphoid tissues of that structure.

In a certain number of cases ordinary appendicitis may complicate the onset of typhoid fever. It is not improbable that in these cases the specific lesions as in the cecum and the consequent interference with drainage of the appendix may have an important part. The manifestations are similar to those met with independently of typhoid fever, but it may be said that, as a rule, these cases usually pursue a relatively benign course and become quiescent or are resolved.

Acute intestinal obstruction may in the beginning suggest appendicitis. The early development of indications of more or less complete intestinal obstruction with marked distention and without the usual evidences of inflammation found in appendicitis, will aid in the distinction.

Acute pancreatitis, the rupture of a gastric or duodenal ulcer, and *acute peritonitis* following rupture of ulcers of other parts of the intestinal tract, suggest appendicitis in the suddenness of onset, the intense abdominal pain, the tendency to nausea and vomiting, the occurrence of fever, and in the constitutional condition of the patient. The localization of the symptoms and the profound character of the disturbance, especially the speedy development of early collapse, enable one to arrive at a proper diagnosis, in the majority of cases, before the condition has proceeded to its more pronounced grades.

Pneumonia.—Not rarely the pain in the early stages is referred to the abdomen, especially in children, and the resemblance to appendicitis may be so puzzling that operation is undertaken. A careful physicial examination will, in most instances, prevent this error; but there are cases in which, owing to the lateness of the appearance of distinct physical signs, the diagnosis of pneumonia may be difficult.

Malaria.—Attention has been called to the occasional onset of malaria with abdominal symptoms. In these cases the occurrence of a rigor and sudden fever, with intense abdominal pain, suggests appendicitis. There may even be rigidity and localized tenderness. In some instances the diagnosis has been possible only after an examination of the blood.

Cholecystitis.—The pain may be referred to the lower right quadrant of the abdomen, and whatever tenderness is discovered may be most decided in the same region. The symptoms of onset may be practically the same as those of acute appendicitis. On the other hand, in cases of appendicitis, the pain may be referred to the region of the gall-bladder; or, when the appendix lies posterior to the cecum, it may be most marked in the back, posterior to the liver. Difficulty in diagnosis may, therefore, arise from the mistaking of cholecystitis for appendicitis, or the reverse. Usually the location of the pain and other symptoms and the discovery of tenderness and swelling in the region of the gall-bladder or in the right iliac fossa, make a proper diagnosis possible.

When empyema of the gall-bladder has followed a cholecystitis the tumor or mass may be found in a relatively low position, owing to the gradual increase in the size of the gall-bladder. Pain and tenderness are also situated in a lower position than is usual in the acute stages of cholecystitis. As a rule, however, the mass can be found to have a certain pyriform shape and to be dependent from the under surface of the liver; and the point of maximum pain or tenderness is usually above the transverse umbilical line.

Biliary colic simulates appendicitis in the suddenness of its onset, the intensity of the pain, and the associated rigidity of the abdominal muscles, together with nausea and other gastric symptoms. As in other hepatic and biliary conditions, however, the pain is situated higher up; and the development of jaundice is an important distinctive indication. Intense and repeated vomiting is never as frequent in biliary colic as in the average case of appendicitis.

Biliary cholelithiasis without definite attacks of biliary colic has often been mistaken for subacute or chronic appendicitis. The frequent occurrence of slight or severe pain in the right half of the abdomen, not rarely referred to the lower right quadrant, and the tendency to disturbance of the intestinal tract and to more or less gastric disorder, are suggestive. Not infrequently, an enlargement of the gall-bladder is present. Suggestive tenderness in the region of the gall-bladder is one of the most important signs upon which a diagnosis may be made.

Nephrolithiasis and Renal Colic.—In acute attacks of renal colic the intense pain radiating from the loin to the external genitalia and disturbances in micturition are of special importance. When a calculus has worked its way to the lower portion of the ureter and has become fixed in this position it may occasion acute attacks which are most difficult to distinguish from appendicitis. The pain and localized tenderness, if the right side is affected, may be in the region of the appendix, and show less tendency to radiation downward. The character of the pain, however, is often of a distinct cutting nature; disturbances of micturition, the appearance of crystals or blood in the urine, and finally the result of roentgen-ray examination, may establish the diagnosis. It should be remembered that hematuria has been known to accompany appendicitis.

Acute pyelitis and other inflammatory conditions of the kidney may be attended with considerable pain, and may simulate appendicitis; it is sometimes very difficult to differentiate between acute pyelitis and

inflammation of a retrocecal or extracecal appendix. The pain and tenderness may be similarly located in the two conditions and occasionally temporary blockage of the ureter in pyelitis may prevent the appearance of pus cells in the urine. Usually, the situation of the pain, the tenderness in the loin and perhaps enlargement of the kidney, and the results of an examination of the urine, make the diagnosis possible.

Movable kidney has been mistaken for appendicitis, the sudden occurrence of painful attacks (Dietl's crises) being the principal occasion of confusion. These attacks may be indistinguishable from the cramp-like pains of a beginning appendicitis. A careful examination usually makes the diagnosis possible by discovering the movable enlarged kidney. The greatest difficulty occurs when the abdominal walls are sufficiently thick to prevent careful palpation, or muscular rigidity is unusually pronounced. Among the distinguishing symptoms the most important are those arising from disturbance of micturition.

Acute peritonitis from various other causes may simulate appendicitis. Thus tuberculous peritonitis, or peritonitis following perforations of the intestines or other hollow viscera, or consequent upon extension of pelvic infection, may resemble appendicitis even on most careful examination. Preceding conditions, the location of the symptoms, the early evidence or more or less extensive involvement of the peritoneum, and the absence of the more or less localized involvement of the right iliac region, enable the physician to arrive at a correct diagnosis.

Salpingitis and *oöphoritis*, with or without localized peritonitis, may offer considerable difficulty in many instances and differentiation between these conditions and appendicitis is a common problem. The frequency of pain in the pelvic region and back, the occurrence of other pelvic symptoms, and the location of the acute tenderness, are suggestive, while the results of vaginal examination usually give a correct diagnosis. The early development of a localized peritonitis in these cases increases the difficulty, especially when the history of the earlier symptoms cannot be obtained or is uncertain. The occurrence of acute appendicitis with acute tubo-ovarian inflammation has been observed.

Acute abdominal symptoms in *angioneurotic œdema* and *Henoch's purpura* may simulate appendicitis.

Ovarian Pain.—In some patients, particularly in neurotic young women, attacks of intense pain in the right lower quadrant of the abdomen may occur at the beginning of menstruation, and persist through the whole period. Sometimes these seem to be dependent upon overloading of the cecum, when a certain fulness will be detected on palpation. Moderate fever occasionally occurs. The resemblance to acute appendicitis may be very puzzling especially when nervous mimicry of other symptoms, such as gastric disturbances and muscular rigidity, occurs. A careful study of the general condition, the absence of leukocytosis and of a characteristic clinical course, may establish the diagnosis; but in some cases doubt must remain even after subsidence of the symptoms at the end of menstruation.

Nervous mimicry of appendicitis may also occur in women at other times and perhaps with nearly equal frequency in neurotic males. It

must be remembered that there is a certain degree of physiological sensitiveness at the ileocecal valve which may readily increase under nervous conditions, and abdominal rigidity is not infrequent under the same circumstances. The general indications of infection and local inflammation, however, are wanting, and if the nervous character of the patient is recognized a proper diagnosis is usually easy.

Prognosis.—Although the majority of patients with acute appendicitis recover, the disease must be regarded as one of decided seriousness, because it is often impossible to determine that an unfavorable extension, which may terminate in rapidly fatal peritonitis, is about to take place; and because, in cases of recovery, such after-results remain that recurrent attacks will probably recur.

Treated in a purely medical or tentative manner, the great majority of patients recover. It is impossible to quote exact figures since it is extremely difficult to recognize milder cases with certainty, and sometimes even the severest forms would pass undiagnosed but for the character of the terminal conditions. The greatest difficulty is caused by the fact that there is a very large group of cases of extremely mild character in which pain, slight gastro-intestinal symptoms, possibly moderate fever, and rigidity in the side may occur, but in which the physician may hesitate to make a diagnosis of appendicitis. Practically all these recover, and very many are never classified as instances of appendicitis. The result is that tables of prognosis fail to include at least a large number of instances, and consequently present a less favorable impression than if all were included. Even with this error, which tends to make the outcome of the disease seem somewhat less favorable than it should be, the recoveries from appendicitis treated by ordinary medical means or by expectant methods constitute a very large proportion of the total number of the cases.

Sahli collected 7213 cases, of which 473 were operated on; while 6740 were not. Of the latter group, 91 per cent. recovered. Recurrences took place in 4593 cases; and of these, 3635 recovered without further recurrences. Of course the cases in which operation was performed represented a disproportionately large percentage of the serious cases. On the other hand, cases in which the disease had advanced rapidly and operative measures seemed futile would be classified in the group of those not operated on.

A study of the surgical literature convinces one that the mortality from acute appendicitis treated by prompt and skilful surgical methods is probably lower than that recorded in most of the statistics from medical or expectant methods. In a measure these statistics may be somewhat deceptive in that they fail to include some of the most serious cases in which operation was deemed inadvisable, and, on the other hand, include some cases of doubtful diagnosis. Objections of a similar nature can be urged against statistics pointing the other way.

The liability to *perityphlitis* is always very great. Some instances occur of appendicitis without extension beyond the walls of the organ, but the tendency to extension through the walls or to perforation is extremely great. In those cases in which, as the result of an angulation,

bend, adhesion, or other form of stenosis, temporary interference with drainage occurs when the cecum is distended, mild catarrhal attacks may be met with from time to time, without very great liability to extension. Eventually, however, in these a severe attack may occur and may terminate in the usual manner.

The liability to *diffuse peritonitis* is decidedly less marked than that to perityphlitis. The mode of extension of the infection is such, and the reactive process in the neighboring peritoneum so prompt, that limitation of extension is usually brought about by the agglutination of neighboring coils of intestine and the formation of a restraining wall of more or less firmness. It is unfortunate that no method of diagnosis enables the physician to determine the existence of conditions that may lead to the sudden rupture of an inflamed or a necrotic appendix.

The liability to relapse after recovery from acute appendicitis is very great, although it cannot be accurately estimated in figures. There are many instances of recovery with no subsequent tendency to recurrence, especially in those cases in which a total obliteration occurs. The usual manner of recovery is by the formation of more or less fibrous thickening or adhesion, and such conditions predispose to subsequent reinfection.

Treatment.—It is difficult to state in a categorical manner whether this should be invariably surgical, or only in selected instances. Medical men, as well as surgeons, recognizing that it is often impossible to determine when an apparently benign case will terminate in sudden extension or rupture, with the development of peritonitis, believe that it is usually wiser to regard every case of appendicitis as demanding surgical treatment. A few years ago it was urged by many surgeons that every case in which the diagnosis had been established demanded immediate operation, unless some unusual contra-indicating circumstance prohibited that method of treatment. This attitude was supported by statistical evidence that seemed to show that, taken all in all, more patients would recover if all were subjected to immediate operation than if an attempt were made to select those in which operation was desirable and to postpone operation in other cases. However much it may be urged, on the ground of statistical evidence, that every patient with appendicitis should be subjected to immediate operation, nearly all physicians and surgeons of experience do hesitate in certain cases with mild and perhaps doubtful symptoms, and sometimes even in cases of frank although not threatening character, preferring to await the development of more definite evidences or of more imperative indications for operation in the hope that, when the inflammation has become limited or has subsided, the safer interval operation may be performed. Moreover, some surgeons advocate delay in some cases of appendicitis with spreading infection. This view was formerly advocated mainly by European surgeons.

It happens, therefore, in practice that among any series of cases a certain number will be regarded by both the physician and the surgeon as proper cases for non-operative treatment. In other instances the existence of some complication or coincident disease of a prohibitive character may prevent operation; and finally, certain patients positively refuse operation when it is proposed. Leaving out these exceptional cases the only safe plan is immediate or prompt operation.

Medical Treatment.—The first appearance of symptoms suggestive of appendicitis demands immediate rest in bed and the utmost possible relaxation of the patient. In many cases the character of the symptoms of onset is such that the administration of a purgative may seem indicated. In view of the possibility of an acute appendicitis, the physician should in such instances select gentle measures. Enemata are more desirable than purgatives; and of the latter, small doses of calomel, or the cautious use of salines at short intervals until effective, are preferable to a single large dose of the same remedies or to more active purgatives. After symptoms definitely indicative of appendicitis have appeared, the use of purgatives, even of the milder sort, requires careful consideration. The opinion of most surgeons is opposed to their administration. Perhaps such a generally sweeping rule is unwarranted. There are cases of mild type with constipation and retention of feces or gas in the cecum and colon in which gentle purgation is both satisfactory and effective. The free evacuation of the bowel may reëstablish adequate drainage and cut short an attack that might otherwise proceed to a more serious extent.

Pain is one of the symptoms that usually requires special consideration. In the beginning, when the nature of the pain is doubtful, warm applications, such as large fomentations, hot-water bags, poultices, or stupes may relieve pain as well as gastric irritability. When the symptoms have become more localized in the region of the appendix, applications of cold are preferred, because of a possible controlling influence on the inflammation itself and because they are rather more effective in controlling the pain. Ice-bags, cloths moistened with ice-cold water, ice poultices, etc., may be employed.

The use of *opium* has been generally discredited because of its tendency to mask the symptoms and because in case of subsequent operation it so interferes with peristalsis as to complicate seriously postoperative conditions. Sometimes, however, despite theoretical and practical objections, the degree of pain is so great that small doses of opium are demanded when the diagnosis is still in doubt or when operation is contra-indicated. Certain surgeons advocate minimal doses, even in cases in which the diagnosis has been made and operation is contemplated. In no circumstances should this drug be used in large amounts.

Occasionally, when gastric irritability, meteorism, and general intestinal colic are conspicuously associated with the other symptoms, carminatives, such as spirit of chloroform, Hoffmann's anodyne, menthol, oil of peppermint, phenol, etc., may give relief. Excessive gastric irritability may be controlled by small doses of cocaine, phenol, dilute hydrocyanic acid, cerium oxalate, or aromatic spirit of ammonium. In some cases in which operation cannot be performed, or in postoperative gastric distention and distress, lavage will occasionally put an end to troublesome or threatening symptoms.

Diet.—In the beginning stages, all food, and even water, should be withheld. If excessive thirst is complained of, small pieces of broken ice may be allowed; or, after evacuation of the lower bowel, enemata of warm water may be given. If acute symptoms have subsided after forty-eight hours, a cautious return to liquid diet may be advisable.

Milk or broth, 1 dram to ½ ounce, may first be given, and increased as the tolerance improves. A return of local symptoms, fever, or gastric disturbance should suggest the immediate withdrawal of food.

Treatment of Chronic Appendicitis.—Cases in which a history pointing to one or more previous attacks of appendicitis is obtained, and in which local symptoms and physical signs or disturbances of bowel function indicate the probability of adhesions, thickening, angulations, or other chronic alterations in and about the appendix, must be carefully considered with reference to the desirability of operation in the interval before the occurrence of another acute attack. When the diagnosis is certain, operation should be unhesitatingly recommended; and even if somewhat uncertain, operation is the safer plan when the occupation or life of the patient is liable to take him beyond the reach of immediate surgical aid should another acute attack occur. The risk from operation in the interval is exceedingly small, but the slight danger incident to general anesthesia, the possibility of other accidents in the course of or following the operation, and the danger of postoperative hernia (not to mention the other undesirable features connected with an unnecessary operation) should prohibit exploratory incisions in cases with doubtful, even though somewhat suggestive, symptoms. It is better to await developments. Operations are sometimes recommended in cases in which obstinate abdominal symptoms of obscure character have occurred. Exploration will more likely fail than succeed in revealing any chronic disease of the appendix. In the great majority of cases chronic conditions of the appendix furnish sufficiently clear indications to establish at least a presumptive diagnosis.

TUBERCULOSIS OF THE APPENDIX

Tuberculosis of the appendix is occasionally met with at operations and at autopsy. It is said to be found in 2 per cent. of the operation cases (Lockwood). The condition is, like other forms of intestinal tuberculosis, usually secondary to tuberculosis of the lungs. It may occur independently of other involvement of the intestines, but is more commonly found in association with tuberculosis of the cecum. In a few instances primary tuberculosis of the appendix has been met with. The lesions are of variable character. Usually there is a simple tuberculous ulceration; in other cases, extensive invasion of the walls of the appendix, with secondary caseation and pus-formation, may be found; while extensions to the peritoneum, in the form of miliary tubercles, or a more diffuse localized peritonitis, may be seen. Crowder has described a case of primary hyperplastic tuberculosis limited to the appendix, and similar to hyperplastic tuberculosis of the cecum (*q. v.*).

Symptoms.—These may be indistinguishable from those of ordinary appendicitis; and a large number of the cases that have been reported have been discovered upon surgical operation for supposed appendicitis. In some cases a suspicion of the nature of the process might arise from the fact that there is, at the time, decided enlargement of the regional

lymphatic glands. A case of this sort occurred in the experience of the writer, and the nature of it was readily recognized before operation. In some cases secondary tuberculous abscesses form.

ACTINOMYCOSIS OF THE APPENDIX

A number of instances of this condition have been reported. The symptoms are those of a sudden or gradually developing lesion in the right iliac fossa, with the development of persistent soreness and a tender swelling. Rarely the process remains limited to the appendix. Usually it tends to spread to the neighboring structures.

CYSTIC DISTENTION AND MUCOCELE OF THE APPENDIX

Retention cysts of the appendix are not uncommon. They result from the gradual transformation of the contents of the appendix, in cases of obstruction of its mouth or of obstruction of its lumen, into liquid of a serous or watery character. Considerable dilatation of the distal portion of the appendix may occur, and a cyst of sufficient size to be detected through the abdominal walls may be formed. The wall of the appendix suffers attenuation, and sometimes hernial protrusions of the mucous membrane between the separated fibres of muscularis may be seen. In most instances such dropsical cysts have been found at operation or at autopsy, not having been suspected during life. In some cases operations have been undertaken for suspected abdominal or pelvic tumors, and the condition described has been found.

Mucocele.—This is a condition in which the appendix is found distended with grayish or whitish gelatinous material of a mucoid character. In some instances this may be the result of an inflammatory condition resulting from occlusion; in other cases the histological features suggest a neoplastic process. In some of these cases the condition was found in association with papillomatous disease of the ovary.

TUMORS OF THE APPENDIX

Polyps.—Rarely polypoid outgrowths from the mucous membrane occur in the appendix as in other situations.

Myxoma.—One instance, shown by Churton and removed by Mayo-Robson, is referred to by Kelly and Hurdon.

Myoma.—A few instances are described in the literature. Small nodular masses, about 5 mm. in diameter, occurred in the case described by A. O. J. Kelly. There was chronic inflammation of the appendix.

Malignant Tumors.—*Primary carcinoma* of the appendix occurs more frequently than is commonly believed. Kelly and Hurdon collected 49 cases, including 2 designated as endothelioma. In most instances in which the situation was noted the growth occurred at or near the tip. Reimann reported primary carcinoma in 0.13 per cent. of 13,651 appendices examined, the majority being in females. The tumor is usually small, having been in 15 cases from 5 to 12 mm. in diameter, but may be

the size of a walnut. The gross appearance may be that of a fibrous tumor. Sometimes it has presented caseation, and has suggested tuberculosis. The neoplastic tissue may not be evident on gross inspection. Microscopically, the appearances are those of a glandular intestinal carcinoma. Sometimes infiltration as far as the meso-appendix occurs; 9 of the 11 cases studied by Kelly were of this description. Carcinoma of the appendix is somewhat peculiar in the early age at which it presents itself. Of 25 instances of primary carcinoma, 4 occurred under twenty years of age, and 11 between twenty and thirty years. The youngest reported case is that of a girl, aged twelve years.

The clinical symptoms are practically indistinguishable from those of chronic appendicitis or of appendicitis with perforation. A fatal termination may be due to perforation and secondary peritonitis. Periappendicular abscesses are not uncommon. Extension of the carcinomatous process to surrounding structures occurs in a certain number.

The *prognosis* after removal has not, as yet, been certainly determined, because the time that has elapsed since the first operation for this condition was undertaken is relatively short. Halsted's patient, according to Kelly and Hurdon, was living five years after operation.

Secondary carcinoma of the appendix is occasionally met with, especially in association with carcinoma of the pelvic organs.

Sarcoma.—Sarcoma has been found in a few instances.

TUBERCULOSIS OF THE INTESTINE

Intestinal tuberculosis may result from the ingestion of tuberculous meat or milk (primary intestinal tuberculosis), as distinguished from secondary intestinal tuberculosis, which results from an infection of some part of the intestinal tract from a previously existing focus. This is, in most cases, pulmonary tuberculosis, the intestinal lesion usually resulting from the swallowing of bacillus-bearing sputum. Less frequently secondary tuberculous enteritis results from the extension of a tuberculous focus in the peritoneum, the abdominal lymph nodes, or one of the abdominal viscera.

Concerning the relative frequency of primary and secondary intestinal tuberculosis, Zahn[1] places the occurrence of primary intestinal tuberculosis at 2.27 per cent., while Ciechanowski,[2] on the basis of 13,203 autopsies, figures it at 1.04 per cent. Secondary intestinal tuberculosis Zahn found in 63.21 per cent. of cases of pulmonary tuberculosis, and Stewart found intestinal involvement in 18 per cent. of 560 cases with pulmonary lesions. The results of the investigations on the frequency of tuberculosis, especially of the digestive tract, in children dying of diphtheria are interesting. Among 714 cases dying of diphtheria Heller[3] found tuberculosis in 140 (19.6 per cent.), in 53 (7.4 per cent.) of which it was primary in the digestive tract. Councilman, Mallory, and Pearce[4] in 220 cases found tuberculosis in 35 (16 per cent.), in 13

[1] *Münch. med. Wochenschrift*, 1902, Nr. 2, p. 49.
[2] *Wien. klin. Wochenschrift*, 1907, Nr. 37.
[3] *Deutsch. med. Wochenschrift*, 1902, Nr. 39, p. 696.
[4] *Diphtheria*, Boston, 1901.

(5.9 per cent.) of which it was primary in the digestive tract. Among 806 diphtheria cases Baginsky found 144 (17 per cent.) to be tuberculous, and in only 6 (0.7 per cent.) was it primary in the digestive tract.

Although the commonest lesion of intestinal tuberculosis is the tuberculous ulcer, other processes may present themselves either in conjunction with ulceration or independent of it. Certain clinical distinctions may differentiate the ulcerative, the stenotic, and the hyperplastic varieties. Clinically, it may be found difficult to classify all cases strictly according to these types, and frequently combinations exist.

Tuberculous Ulcers.—The most frequent localization of tuberculous ulcers is in the ileum just above the ileocecal valve. They occur, however, as high up as the duodenum and as low down as the rectum. The ulcer usually begins in a solitary follicle or Peyer's patch, although it may occur in the mucous membrane itself. It commences as a small, shot-like, gray nodule just below the mucous surface. This enlarges and later its centre undergoes caseation. Finally, the entire nodule becomes caseous and subsequently breaks through the overlying mucous membrane, the caseous material is discharged into the bowel, and the tuberculous ulcer results. At this stage it has a small, crater-like opening, elevated caseous edges, and a caseous base. Frequently a number of these primary ulcers unite to form a larger ulcer. In other cases the larger ulcers result from the simple increase in size of the single original ulcer, by the caseation of miliary tubercles deposited about its margins. Since this extension is by means of the lymph channels, the longest diameter of the ulcer is usually at right angles to the long axis of the intestine, and at times the ulcer extends as a girdle about the entire lumen of the bowel. The margins are elevated, irregular, and usually slightly undermined. Frequently tubercles can be seen with the naked eye in the elevated thickened edges. The peritoneal coat of the ulcer is usually thickened, of a dark, bluish-gray color, and frequently contains miliary tubercles. At times the peritoneum corresponding to the area of ulceration is covered by a fine exudation that may lead to adhesions between adjacent coils of intestines.

Terminal Changes.—Complete healing with the disappearance of all tubercles is unusual. The ulcers frequently undergo partial organization, so that while some ulceration remains, a moderate degree of stenosis is also present. Perforation is seldom a complication of tuberculous ulceration, except in the rectum. Two factors tend toward this infrequency: the thickening of the peritoneal covering and the tendency to the formation of peritoneal adhesions. It is consequently especially in young, rapidly progressive ulcers that the tendency to perforation is greatest. If perforation occurs, either a general peritonitis results, or, if adhesions between adjacent coils of intestines have formed, walling off the seat of perforation, a localized peritoneal abscess results. On account of the fact that the ulcers are most frequent about the ileocecal valve and usually most advanced in this area, the site of the perforation is relatively most frequently found in the right iliac fossa, or in the pelvis where the coils of the lower ileum usually lie. Occasionally multiple perforations have been found. Perforation has been known to occur

into neighboring organs, as the bladder or uterus. Ulcers in the rectum not rarely perforate and cause ischiorectal abscesses. Carcinoma has been known to develop in the site of an old tuberculous ulcer.

Symptoms and Diagnosis.—The symptoms of ulcerative tuberculous enteritis do not differ materially from those of simple enteritis or of other forms of ulceration of the bowels. The most constant and characteristic symptom is diarrhœa, but this is by no means invariably present even with quite extensive ulceration. The stools are either soft and unformed, although presenting no special alteration from the normal in other respects, or thin and watery. Mucus may be found in small masses, or as strings or shreds, especially in the cases in which the feces are semisolid. There may be admixture of blood in small quantities, and occasionally considerable hemorrhage occurs. When formed stools are passed, or when the feces are hard from constipation, they may be coated with blood-streaked mucus and pus, provided the ulceration is situated in the lower bowel. Continued diarrhœa causes rapid emaciation and loss of strength, although occasionally the patient maintains his flesh and strength surprisingly. Soreness and localized tenderness are not usually marked unless extension to the peritoneum has occurred. Ordinarily the temperature is not much influenced and any fever is usually due to the primary pulmonary lesion.

Since the symptoms do not differ materially from those of most of the chronic inflammatory and ulcerative conditions in the intestines, the *diagnosis* must rest to a great extent on the associated phenomena. Due attention must be paid to the fact that in children primary intestinal tuberculosis is much more common than in adults, and that more than 50 per cent. of the cases of pulmonary tuberculosis in adults are complicated by intestinal ulceration. Consequently the occurrence of diarrhœa and other symptoms of enteritis in an adult suffering from pulmonary tuberculosis would justify strong suspicions of the existence of intestinal ulceration. At the same time amyloid disease of the intestines is a common complication of tuberculosis. The diarrhœa of amyloid disease is usually more watery than that of tuberculous enteritis, and is less commonly associated with the presence of occult or visible blood.

In children the diagnosis is usually more difficult than in adults. A persistent diarrhœa, with progressive wasting, abdominal pain and distention, and enlarged glands without determinable cause, would warrant a tentative diagnosis of tuberculous enteritis. In both adults and children the diagnosis is greatly strengthened by the discovery of tubercle bacilli in the stools. When infected sputum is swallowed tubercle bacilli may be found in the feces before an intestinal lesion has occurred.

Stenosing Tuberculous Enteritis.—Stenosis of the intestines of tuberculous origin without ulceration results when the tendency to organization as a result of the inflammation exceeds the tendency to destruction of tissue. It is by no means frequent. A distinction must be made between those cases in which stricture has succeeded upon ulceration and those in which the stenosis is the primary and predominating feature. The latter constitutes the type now specially under discussion. The tuberculous nature of these strictures is sometimes determined only with the

greatest difficulty and in the past many of these cases may have been looked upon as syphilitic. The strictures are most frequent in the ileum and colon and are usually multiple. The symptoms are those of chronic intestinal obstruction, and the tuberculous nature of the condition can be diagnosed only by the associated lesions or by exclusion of other etiological factors. The tuberculin reaction may be of assistance.

Chronic Hyperplastic Intestinal Tuberculosis.—This is characterized pathologically by varying degrees of stenosis and ulceration, but primarily by a proliferation of tuberculous granulation tissue in the intestinal wall. This leads to a great increase in thickness of the wall and consequent stenosis, which produces one of the predominating clinical manifestations. The condition may originate in either the mucosa or the serosa, and is usually secondary to tuberculosis elsewhere. Its almost invariable site is the ileocecal region. The predominance of the hyperplastic over the destructive processes is probably a result of decreased virulence of the tubercle bacillus.

According to Conrath the majority of the cases occur between the ages of twenty and forty years. The active symptoms are preceded by a long duration of vague, rather mild intestinal disturbances. Not until the stenosis is sufficient to produce symptoms of obstruction is diagnosis possible. These obstructive symptoms are of insidious onset and form one of the most constant features. A tumor presents itself sooner or later, and the resemblance to carcinoma is often marked. Obrastzow looks upon the slow and late development of the stenosis as pointing to tuberculosis rather than to carcinoma. The mass usually has a cylindrical form, giving the impression of a greatly thickened intestinal wall. Occult blood is usually present in the stools, and frequently the feces contain visible quantities of admixed blood. Fever usually occurs. The diagnosis is substantiated by tuberculosis elsewhere or by the discovery of tubercle bacilli in the stools.

Treatment of Intestinal Tuberculosis.—The prevention of intestinal infection is to some extent possible. Patients suffering from pulmonary tuberculosis should be made to realize the danger of swallowing sputum. Unfortunately, this occurs during sleep and cannot then be prevented. The main purpose of treatment after ulceration has occurred should be to save the patient's strength by controlling diarrhœa and as far as possible the ulceration itself. There is some tendency toward healing, but the object is not so much to secure this result as to control the waste of the patient's vitality. Careful regulation of the diet is an essential. This may necessitate some diminution in the amount of food but careful consideration is necessary to decide whether it is wisest to limit feeding on account of the bowels or to continue overnutrition on account of the pulmonary and general infection. No set rules can be laid down. Pasteurization or predigestion of the milk is often desirable. General hygienic measures, fresh air, rest, and especially direct exposure to sunlight, are of great importance. Recently encouraging results have been reported from quartz-lamp and sunlight therapy.

So far as remedies are concerned, it is always well to use those that are least likely to disturb the stomach. Small doses of bismuth subnitrate,

subgallate, or salicylate given rather frequently and continued for some time may have a useful effect. Among the antiseptics, guaiacol carbonate, creosote, carbolic acid, ichthyol, or iodoform may be used. When diarrhœa is excessive, small doses of nitrate of silver, acetate of lead, and vegetable astringents may be administered temporarily or until the bowels become more settled. Sulphur seems to exercise a useful effect in some cases. When ulcers are found in the rectum, direct treatment may aid healing and prevent extension to the perirectal tissues.

The stenosing and hyperplastic forms demand surgical treatment if the symptoms are pronounced and the condition of the patient permits of operation. The results in some cases have been very satisfactory.

SYPHILIS OF THE INTESTINES

Intestinal lesions of syphilis are rare. They occur in both congenital and acquired syphilis but are more common in the former. The intestinal lesions of congenital syphilis are always associated with syphilitic phenomena in other organs. They usually take the form of multiple small gummata, and are found almost solely in the small intestines, and especially in the ileum. They take the form of flat, grayish elevations. Superficial necrosis frequently occurs, leaving an ulcer with a fibrous base and very slightly elevated edges. The ulcers usually extend in a direction at right angles to the axis of the bowel, and at times lead to stenosis. Perforation of a syphilitic ulcer has been reported.

In acquired syphilis, symptoms of enteritis at times occur early in the disease, which may be of the nature of intestinal manifestations comparable to the secondary cutaneous manifestations. Pathological observations of the condition are wanting. Later in the disease intestinal lesions are observed similar to those observed in congenital syphilis, excepting that they are more common in the large intestine than in the small. They appear first as grayish-red, smooth, gummatous elevations, which later undergo necrosis resulting in flat, sharply marginated ulcers, with a smooth, translucent, gray or yellow base. As in the congenital lesions, they tend to extend around the lumen of the bowel and cicatrize, thus producing stenosis. Occasionally perforation occurs.

The most frequent situation of syphilitic ulceration of the intestines is in the rectum and particularly in its terminal portion just above the sphincter. The ulcers are distinguished from those of dysentery by their smooth, gray base and the tendency to induration of the edges and extensive stenosis. It is probable that stenosing tuberculous ulcers of the rectum have been frequently mistaken for syphilitic lesions. Syphilitic rectal stenoses are more common in women than in men. They may result from the cicatrization of a primary lesion, of mucous patches, or of ulcers caused by necrotic gummata.

The *symptoms* of syphilitic involvement of the intestines are those of simple intestinal ulceration or stricture and permit a probable diagnosis only on the basis of the history or the associated findings of syphilis, and possibly their response to the therapeutic test. Syphilitic stenoses

of the rectum are distinguished by the marked induration and extensive cicatrization.

The *treatment* is directed to the general infection and to the control of the diarrhœa. The latter often persists in spite of ordinary treatment and until active antisyphilitic remedies are employed.

AMYLOID DISEASE OF THE INTESTINES

This occurs as a result of the same causes that produce amyloidosis elsewhere. The most prominent causes are chronic tuberculosis, syphilis, chronic suppuration, and the various cachexias. In point of frequency, the intestines stand fourth among the organs affected, the kidneys, spleen, and liver being the organs more frequently involved. Usually the entire intestinal tract is diffusely affected, but at times the ileum only is the seat of the disease. More rarely the colon alone is affected. The process may involve any or all of the tissues composing the intestinal wall, but seldom affects the mucous membrane itself. The lymphoid follicles usually remain entirely free from the amyloid involvement. The diseased intestine presents a pale, shiny, translucent appearance, and gives the typical amyloid reaction.

A feature of amyloid disease of the intestines requiring special mention is the so-called *amyloid ulcer*. These vary in size from that of a pin-point to that of large areas involving the entire circumference of the intestines in a girdle-like fashion, and from 5 to 15 cm. in length. They have smooth, slightly thickened edges and a pale base with numerous small striations. It is possible that a simple ulceration occurs as a result of the insufficient nutrition of the surface epithelium caused by the amyloid degeneration of the underlying vessels. It is possible that some ulcers described as amyloid were tuberculous ulcerations occurring as one of the manifestations of the disease producing the amyloidosis.

Mild degrees of amyloid disease present no *symptoms* by which it can be recognized clinically. More severe grades present one constant feature—diarrhœa. The stools are moderately frequent and watery, but present no characteristic features. The cause of this watery diarrhœa has been variously attributed to anemia of the intestinal wall, to increased permeability of the vessel walls, and to decreased absorptive powers of the intestinal mucosa. The question of the presence of blood in the stools in amyloidosis of the intestines is one of considerable importance. Colberg, claiming amyloid ulcers to be a common association of diffuse amyloid disease of the intestines, looks upon the presence of blood in the stools as a diagnostic feature. The probabilities are, however, that the presence of blood in the stools points to the existence of other conditions than simple amyloidosis. Pain and tenderness play no part in the symptomatology of uncomplicated amyloid disease of the intestines. The *treatment* resolves itself into that of the primary disease and an attempt to control the diarrhœa, which is best accomplished by the mineral and vegetable astringents and opium.

INTESTINAL OBSTRUCTION

Definition.—The term intestinal obstruction is here used to signify incomplete or complete interference with the onward movement of the intestinal contents and their eventual discharge, occasioned by some form of mechanical or structural impediment of more or less limited extent. The term does not apply to interference with the passage of the intestinal contents caused by the general weakness or paralysis of the bowels or by the conditions of the contents themselves. A variety of terms have been introduced to designate different kinds of obstruction:

Ileus is an ancient name, variously applied to paralytic conditions of the intestines, to obstruction in a general sense, or to obstruction with feculent vomiting. It is rarely used at the present day, and on account of its indefiniteness should be abandoned.

Occlusion implies a complete closure of the intestinal lumen.

Stricture signifies a contraction of the lumen caused by disease of the wall, usually involving its entire circumference in a more or less limited section.

Constriction signifies a narrowing by adhesions, fibrous bands, or similar conditions outside the bowel.

Obturation signifies an obstruction of the lumen of the intestines by contents, foreign bodies, or other conditions inside the bowel.

Compression indicates obstruction due to the pressure of tumors, misplaced organs, or other conditions outside the bowel.

Incarceration indicates an obstruction, more or less complete, from the retention of a coil of intestine beneath fibrous bands, within hernial sacs, etc.

Strangulation indicates the constriction of a coil of intestine in which more or less complete obstruction of the bloodvessels supplying this coil has taken place, causing intense venous stasis.

Intestinal obstruction may be acute or chronic. Frequently, after partial chronic obstruction, there is an acute increase of the obstruction, and clinically, difficulty is experienced in distinguishing such cases from acute obstructions.

General Pathology.—Certain conditions affecting the bowel and its immediate connections, the peritoneum, the mesentery, etc., result from obstructions of all sorts without reference to the precise morbid condition that has occasioned the obstruction. Characteristic differences are met with in the anatomical conditions occurring in chronic cases, as contrasted with those of acute character.

Chronic Obstruction.—A striking contrast is seen in the bowel below and above the point of obstruction. Below the obstruction the intestinal coils are empty and contracted, and their color more or less grayish or white. The condition is that seen in the empty intestine of persons who have died of inanition. Remnants of the intestinal contents may remain in the contracted bowel below the obstruction. especially when hardened fecal masses had been present at the time of the obstruction and could not readily be transported onward. Above the obstruction the bowel is distended, and, after a certain length of time, elongation, thickening

from hypertrophy of the walls, ulceration, and other inflammatory changes in the mucous membrane and serous coat may be met with.

The first effect is the accumulation of contents above the constricted area, and a resulting dilatation of the bowel. Later, this distention seeks higher and higher levels, until almost the entire intestinal tract above the constriction may be involved. The distended bowel contains fluid or somewhat consolidated fecal matter, according to the situation of the obstruction. In cases involving the small intestine, fluid contents alone are met with. In obstruction of the large intestine there may be semisolid or even solid fecal masses. This, however, is not invariable, as the contents may be fluid even in obstruction of the lower part of the large bowel. A certain amount of gas may be present, but distinct accumulations of gas are unusual, as the gases are absorbed from the mucous membrane so long as the circulation of the bowel has not been seriously disturbed. Moreover, gases are usually able to pass beyond the obstructed area after any onward movement of fluid or solid feces has become impossible.

Hypertrophy of the wall of the bowel follows and this affects the muscularis especially, and may be confined to this part, although some thickening of the other tunics may also occur. Experiments in animals have shown that the hypertrophy begins as early as the fourth or fifth day after obstruction of the bowel has been established, and is quite marked by the ninth day (Herczel). The hypertrophy is due to an increase in the width of the muscle fibres rather than to increase in their number. It is a functional hypertrophy which, to a certain extent, enables the bowel to overcome the obstruction.

Changes in the mucous membrane result from the stasis of the contents and secondary fermentative or putrefactive changes. As a result of the irritation, inflammatory conditions and finally ulceration of the mucous membrane and submucosa occur. Formerly the direct mechanical irritation of retained contents, and especially of hardened masses, was considered of prime importance in the development of such ulcers, and the names stercoral ulcer and decubital ulcer were applied. According to Kocher, a better term would be distention ulcer, as he regards the ulceration as due to overdistention of the intestines with consequent disturbance of circulation. When inflammatory changes are pronounced the mucous membrane may be somewhat thickened, but nearly always it is thinner than normal. The serous coat is thinned by the distention, and more or less stretched in a longitudinal direction as the result of a shortening of the mesentery by the dilated bowel.

Acute Obstruction.—When this has followed a chronic but only partial occlusion, more marked distention of the bowel above the obstruction occurs as the result of suddenly increased pressure and interference with the movement of the contents, causing the accumulation of gases.

In purely acute cases there are quite marked differences from those met with in chronic obstruction. Below the obstructed area the bowel is empty and contracted, as in chronic cases. Above the obstruction the principal change is distention, with great thinning of the walls of the bowel and no evidence of hypertrophy. The contents of the bowel

are, in the beginning, liquid or semiliquid, but after a relatively short time gaseous accumulations occur as a result of interference with the circulation and consequent cessation of absorption from the mucous surface, and also as a result of the inability of the gases to pass the acutely obstructed portion. Paresis of the bowel is favored by interference with the circulation and a hyperemic condition of the walls of the gut. When complete stasis of the circulation has developed, absorption of accumulating gases ceases and increasing dilatation occurs. The gases are partly derived from the air swallowed with food and in part from fermentative processes. A considerable part of the distention may be due to carbon dioxide from the venous blood.

The condition of the bowel in strangulated coils is of particular importance. The obstruction of the circulation in such portions produces a rapid hyperemia, and eventually a complete stasis of the circulation. The coil becomes of a deep red or purplish color and is tensely distended. Hemorrhagic extravasation may occur within the lumen or on the outside. A gangrenous condition may develop, when the intestine becomes of a greenish or grayish color. Occasionally obstruction of the arteries as well as of the veins may cause a somewhat different appearance, the bowel in these cases remaining flaccid and becoming gangrenous in a very short time. The strangulated coil undergoes rapid distention from the accumulation of gases.

Affections of the peritoneum may occur in cases of strangulation or in other forms of intestinal obstruction due to the escape of microorganisms through the wall of the bowel in the area of obstruction, or immediately adjacent to it. The local conditions (compression of the tissues by bands, intussusception, etc.) and the complete stasis of the circulation cause degenerative changes in the wall of the bowel and make them more readily permeable, and thus a rapid involvement of the peritoneum becomes possible. In cases of gangrene and perforation of the intestines a violent local or perhaps general peritonitis quickly supervenes, and foul-smelling collections of inflammatory exudates and necrotic material with escaped intestinal contents are encountered.

Toxemia.—It has been shown that in acute obstruction of the small intestine a toxin is rapidly produced and absorbed. This toxin is probably responsible for the symptoms of prostration and collapse which supervene in such cases, and these symptoms occur more promptly and are more severe when the obstruction is high in the small intestine. Various substances have been found in the contents and mucosa of the obstructed bowel which are believed by different investigators to be the source of the toxemia. Products of protein decomposition (histamine, proteoses, neurin, etc.), alleged by some to be the results of bacterial activity, have been thought to permeate the damaged mucosa and enter the system. Others believe the toxin to be the product, either normal or abnormal, of the intestinal mucosa. There is experimental evidence to support each view.

Coincident with the toxemia there is usually a marked decrease in the chloride content of the blood, and an increase of the available alkali with increased CO_2 combining-power. These changes are followed by a

rise in the non-protein nitrogen of the blood and urine, thought to be due to increased tissue destruction by the toxin. Haden and Orr have thought that the chlorine ions are utilized by the tissues in some way to combat the toxin. They have been able to prevent or lessen the toxemia of obstruction in dogs by administering NaCl, and have recommended its use in man.

The symptoms following obstruction of the fecal current alone have been shown to be much less severe than those produced by interference with the circulation of the bowel (Foster and Hausler). Shock, peritonitis and loss of fluid by vomiting are factors of varying importance in producing symptoms of collapse. Evidence of renal injury from the toxemia of high obstruction has been presented.

General Symptomatology.—The important clinical manifestations of obstruction of the intestines are pain, distention, nausea and vomiting, constipation, prostration, and collapse. A variety of secondary symptoms or variations in the manifestations occurs in the different types.

Pain.—This differs greatly in manner of onset, severity, and character, according to the acuteness of the case. In acute obstruction sudden abdominal pain, usually of considerable violence, is the rule. This may be occasioned by the direct irritation of the nerves in the affected segment, by the sudden compression or obstructive cause, and by the violent peristaltic efforts above the obstruction. As acute obstruction more commonly involves the small intestine than the large, the pain is more likely to be general than localized, as it is well known that the nervous mechanism prevents an accurate localization of pain involving the small bowel. In the majority of cases the pain of onset is referred to the middle portions of the abdomen. At first it is intense and may continue so until, as a result of exhaustion, or possibly of toxemia caused by the absorption of putrefactive products, a cessation is brought about. The pain may be so severe in the beginning that nausea, vomiting, or profound prostration may result. After an interval of cessation, secondary pains of cramp-like or colicky character due to violent peristalsis set in. These, however, are rarely prolonged, as are the pains met with in chronic obstructions. Very soon the bowel becomes fatigued, or prostration reaches a grade that puts an end to the patient's suffering.

Extension of infection to the surrounding peritoneum may add a new form of pain, sometimes distinguishable by its stabbing character and by its association with local tenderness and other symptoms. In other cases rapid abdominal distension may be the occasion of general abdominal pain described as of a rending character.

In *chronic* obstruction, pain may be wanting for a long time, and nearly always its onset is somewhat gradual. The patient first becomes aware of slight abdominal discomfort due, apparently, to some interference with the movement of the contents of the bowel, and especially gases. Later, these sensations increase to a more definitely painful form; or, when there is a sudden increase in the degree of obstruction, intense, cramp-like paroxysms may set in. Not rarely the earlier symptoms have been so indefinite and uncertain that the occurrence of an entirely acute obstruction is suggested. The attacks of pain may become so

severe that the patient screams or doubles up in agony. He is conscious of a more or less fixed location, and may feel the cramps begin at one portion and move more or less quickly to the place of obstruction, where the bowel becomes tensely distended, sometimes forming a visible hard mass. This indurated segment of the bowel may be so hard that on palpation it seems almost like a solid tumor. After a variable duration it relaxes, and relief may be obtained for a greater or less period of time. After a certain duration the colicky pains of chronic obstruction may subside and there may be an interval of hours, days, or even weeks before another attack sets in.

Associated with the paroxysmal pains of chronic obstruction is a symptom of extreme importance, namely, *visible peristalsis*. This may be seen through thin abdominal walls in persons not suffering with intestinal obstruction, but these movements are slow vermicular contractions, visible over a greater or less extent of the abdominal surface. They differ very decidedly from the intense and usually rapid waves met with in obstruction, and on palpation there is never the stiffening and evident tonic contraction found in cases of occlusion.

Meteorism is usually somewhat late in development, except in acute cases with strangulation and rapid interference with the circulation of more or less extensive segments of the bowel. In chronic cases there may be but little distention until near the termination of the case, when complete obstruction has developed and paresis of the bowel above the obstructed area has caused interference with the circulation. Up to the very end the amount of distention may be relatively small. In acute cases, with marked interference of the circulation, rapid and intense meteorism may cause early abdominal distention. In conditions of strangulation of coils of the intestine, paralytic distention of the strangulated area may occasion local meteorism of marked grade.

Constipation.—All forms of intestinal obstruction interfere with the onward movement of the intestinal contents. The resulting conditions vary considerably in different cases. In *acute* obstruction a sudden cessation of all intestinal movements may occasion an immediate absolute constipation, although frequently a movement or two may empty the lower bowel before the constipation becomes absolute. The higher in the intestinal tract the seat of obstruction, the more likely are some movements of the bowel to occur, after the development of the condition. The contents in the bowel below the point of obstruction may be discharged after the obstruction has taken place, and the fluid contents of the upper intestine are more likely to pass a partial obstruction than the semisolid or solid masses of the lower bowel. In partial obstructions in the small intestine continuous diarrhœa with passage of peculiarly offensive stools is not unusual.

In *chronic* obstruction, especially that involving the large intestine, constipation is sometimes absent or insignificant. In these cases the gradual development of the obstruction and the compensating hypertrophy of the musculature above the occlusion make it possible for the contents to escape in an approximately normal manner. Sometimes considerable accumulations of fecal matter may be found above an

area of obstruction in cases in which the movements of the bowels have seemed approximately or wholly normal. Much importance has been thought to attach to the character of the stools in cases of partial obstruction of the lower bowel. Among other forms, small, separated, spherical masses and ribbon-shaped formations, or narrow, pencil-like stools, have been particularly noted. It is undoubtedly true that partial intestinal occlusions do occasion formations of this character; but exactly the same conditions may occur without any organic obstruction whatever, especially in cases of constipation due to local spasm of the bowel, in cases of spastic contraction of the sphincter, etc. The presence of blood, pus, and mucus with the bowel movements is not infrequent in obstructions due to organic conditions involving the lower bowel, especially in carcinoma and intussusception.

Diarrhœa.—This may occur in intestinal obstruction, instead of constipation, and easily occasion a mistake in diagnosis. This is particularly liable to occur in chronic cases and is occasioned by the occurrence of inflammatory conditions of the mucous membrane above the obstruction. Some have believed that diarrhœa is always significant of ulceration, a view that is certainly not invariably correct. The diarrhœa may be continuous and chronic, or may be recurrent. The character of the movements varies, but there is usually a tendency to a considerable admixture of mucus. When ulceration exists, blood and pus may also occur in the movements.

Vomiting.—Soon after the development of intestinal obstruction, whether complete or only partial, nausea and disturbance of the stomach occur, and in many cases vomiting sets in quite promptly. In cases in which there has been marked pain, the nausea and vomiting are in a measure dependent upon the intensity of the suffering, and are clearly reflex. The character of the vomiting varies at different stages. At first the contents of the stomach are brought up, and sometimes, when the stomach has been overloaded at the moment of an acute obstruction, considerable relief follows the primary vomiting. Usually, however, vomiting continues without cessation, and after the food contained in the stomach has been discharged, watery fluid or bile is brought up. Eventually stercoraceous or fecal vomiting takes place, and is the most characteristic symptom. In the beginning the fecal odor is merely suggested. Soon, however, it becomes unmistakable. Finally, quantities of liquid vomit, of the foulest character, are discharged, sometimes with violence, while in other cases it gushes from the mouth.

A great deal of discussion has taken place regarding the *causes* of the fecal vomiting. There is no doubt that antiperistalsis may occur, and that matter in the lower part of the small intestine may be brought to the stomach and vomited. Brinton suggested that, while the ordinary peristalsis carries the contents adjacent to the walls of the bowel forward in the usual manner, a reversed axial current is taking place at the same time. Investigations and a consideration of the functions of the different portions of the intestinal tract, suggest that the symptom is due to the accumulation of secretions in the small intestine, and eventually an overflow. Obstruction in the large intestine, especially when low down, may

be unattended with this symptom or accompanied by it only late in the course, because absorption still goes on in the portion of the large bowel above the obstruction.

Occasionally stercoraceous vomiting may occur in gastro-intestinal diseases, unattended with intestinal obstruction, functional or organic. In these cases bacterial decomposition of gastric contents, and especially of blood mixed with other gastric contents, may cause the odor. The organism most likely to produce this is the *Bacillus coli.*

In cases of obstruction situated near the upper end of the small intestine, the vomiting may be characterized by the intense violence of the straining efforts, by the comparatively small amount of matter brought up, and by the tendency to speedy collapse. In cases of obstruction of the large intestine, and in chronic obstruction generally, vomiting is much less pronounced than in acute cases and those in which the small intestine especially is involved. Sometimes there may even be little nausea until a late stage has been reached, and the vomiting is usually rather closely dependent upon the taking of food, attempts at sitting up, or other movements or efforts. In the late stages, when violent attacks of colic have developed, vomiting of the same character as occurs in acute obstruction develops.

Prostration and Collapse.—In acute cases collapse may set in very promptly. In chronic forms of obstruction it may be absent until the final stages have been reached. The most intense and sudden collapse occurs in cases in which the obstruction is situated high up in the small intestine. It is due to the sudden injury sustained by the nerves of the bowel, and to rapid and severe toxemia, and is proportionate to the pain, retching, and other symptoms caused by the nerve injury. There may be equally sudden prostration and collapse in obstruction lower in the small intestine; but more usually in these cases the patient becomes gradually weaker until finally he passes into a state of collapse. In chronic obstruction collapse may be late, and does not usually present itself until decomposition of retained products and toxemia have occurred.

The *appearance* of the patient suffering with prostration and approaching collapse from intestinal obstruction is often characteristic. The skin is cold, pale, and generally bathed in sweat. The face wears an expression of anxiety and is pinched. The temples appear sunken. The eyes are depressed in their sockets and surrounded with dark rings. The respirations are shallow and often sighing. The temperature of the body falls. The pulse becomes rapid, feeble, and finally thready and irregular. The mucous membrane becomes dry, so that the mouth is literally parched. Urinary excretion diminishes until it may become suppressed. Finally, the patient sinks into a state of torpor, or complete stupor or coma. Before this stage is reached the increasing toxemia and infection cause a cessation of all sensation, and the acute sufferings of the earlier stages subside. Sometimes the obtunding of sensory acuity develops without other manifest evidences of collapse, and may occasion a deceptive appearance of improvement.

The causes of collapse in intestinal obstruction are: (1) intoxication and infection; (2) repeated vomiting and loss of water from the system;

(3) the primary shock to the nervous mechanism of the intestine. The loss of water through vomiting and sweating may operate directly by reducing the strength of the patient, and indirectly by inspissation of the blood. According to Nothnagel, the concentration may reach 24 per cent. of the total volume of blood.

The toxemia of the late stages is doubtless caused by a large variety of substances generated by the decomposition of retained materials in the intestinal tract. Repeated vomiting and consequent inanition may lead to acidosis. Direct bacterial infection adds to the prostration of the patient and coöperates with the toxemic causes of collapse.

Diagnosis.—General Diagnosis.—The existence of intestinal obstruction is usually rather easily determined, when the symptoms that have been mentioned present themselves. In acute cases the sudden occurrence of pain and the development of nausea and characteristic vomiting, the obstinate constipation, and the final prostration or collapse leave little doubt. There are cases, however, in which, although the development of obstruction has been acute, some of these symptoms are poorly developed. On the other hand, there are conditions in which very similar symptoms are occasioned by diseases outside the intestine itself, although doubtless affecting the bowel in an indirect or reflex manner.

Differential Diagnosis between Intestinal Obstruction and Conditions Simulating It.—1. Various conditions may occasion sudden intense pain, with nausea, vomiting, and collapse. Among such conditions are the passage of biliary or renal calculi, the rupture of gastric and duodenal ulcers, torsion of the pedicle of a movable spleen, sudden twisting of a pedunculated subserous uterine fibroid or ovarian cyst, crises in cases of movable kidney, pancreatic hemorrhage and acute pancreatitis, embolism or thrombosis of the mesenteric vessels, and nervous crises associated with locomotor ataxia or other nervous diseases. In all these cases the symptoms of onset may be similar to those met with in cases of intestinal obstruction. If, as a result of the violent irritation of the nervous system, a reflex paralysis of the intestine occurs, an actual intestinal obstruction may develop. Usually, however, in the conditions named, although there is some weakening of motility of the bowels and consequently a certain degree of constipation, the obstruction is not absolute, and enemata rarely fail to bring away a certain amount of fecal matter. Distention of the abdomen, if it occurs, is only of moderate grade. The vomiting, although perhaps urgent in the beginning, does not persist as in obstruction, and rarely is fecal.

2. In a second group intestinal obstruction is suggested by the occurrence of absolute constipation. In a certain sense these cases are truly instances of actual obstruction, although the conditions differ from those of intestinal obstruction in the ordinary sense. In this group may be included the paralytic condition of the bowel following pronounced forms of peritonitis. The onset of such cases, the early development of fever, the leukocytosis, and other evidences of infectious inflammation are important. The vomiting rarely becomes fecal and constipation is not, as a rule, absolute.

In chronic and tuberculous peritonitis, intestinal distention, constipa-

tion, and vomiting may suggest obstructed conditions of the bowel. The clinical course, however, is more prolonged; there is less vomiting than in obstruction, rarely ever fecal vomiting; and the degree of constipation is rarely as great as in obstruction. Direct examination of the abdomen will usually detect local indurations, fluid exudate, or enlarged mesenteric glands.

3. In a third group of cases intestinal obstruction is suggested by the marked degree of abdominal distention, associated with some other, although less conspicuous, symptoms suggesting obstruction. Thus in cases of infectious disease, such as typhoid fever, pneumonia, and violent acute intoxications, and infections of the bowel itself (enterocolitis), progressively increasing abdominal distention, together with nausea, vomiting, and constipation may cause a close simulation of certain forms of obstruction. In these cases, however, vomiting never becomes fecal in type, the degree of prostration and collapse is less pronounced, and the constipation is rarely absolute, so that the use of enemata usually suffices to obtain some fecal discharge.

In the case of certain nervous conditions, notably hysteria, marked distention of the abdomen (phantom tumor) may occasionally occur. In these cases there is often a striking lack of other symptoms, and the distention not rarely varies very quickly. Under psychic influences, and when the patient is asleep or is anesthetized, such abdominal distentions may suddenly subside. Similar distention of the abdomen may occur in patients suffering with locomotor ataxia; but in these cases severe abdominal pain and sometimes associated gastric crises attended with vomiting are more apt to be present.

Diagnosis of the Situation of the Obstruction.—Obstruction in the uppermost portion of the duodenum may present the features of pyloric obstruction. When the occlusion is below the outlet of the bile-duct intense vomiting with constant presence of bile is a striking feature. The vomit does not in this case become stercoraceous. When the point of obstruction is in the jejunum or ileum the gastric symptoms though often marked do not so wholly dominate the symptomatology. The pain is less definitely localized, the vomiting becomes stercoraceous earlier, and suppression of urine is a more marked and earlier manifestation than when the obstruction is situated in the large bowel. Stiffening of segments of the bowel in the central portion of the abdomen and the narrowness of the palpated coils may indicate that the obstruction affects the small intestine. Obstruction in the large bowel usually occasions a more reliable localization of pain and tenderness, and the passage of mucous movements or blood and mucus are significant. When tonic peristaltic contractions of the bowel, with violent attacks of colic, set in, these may sometimes serve to locate the place of obstruction, as the wave of contraction may move indefinitely through the abdomen until it reaches the point of obstruction, where it produces a stiffening from tonic spasm, and sometimes a hard tumor-like mass. This point may be recognized by the patient himself and accurately located by him; or it may be seen through the abdominal walls or felt in palpating the abdomen. Obstructions in the lower part of the large

intestine, especially in the rectum, may occasion ribbon-shaped or pencil-like stools for some time before the obstruction is complete.

Roentgenologic Methods of Diagnosis.—The diagnosis of the site and sometimes the kind of obstruction has been greatly facilitated by these methods, which are particularly available in cases of partial and chronic obstruction. In cases of obstruction in the small intestine or in the upper part of the large intestine, examinations at various intervals after administration of bismuth or barium meals give the best results. When the obstruction is low down in the large intestine, opaque enemata may prove more satisfactory. In the study care must always be exercised to determine whether the point of obstruction is indicated in several plates so as to avoid confusing a temporary stagnation for a fixed condition. Fluoroscopic examinations are particularly valuable in enabling the examiner to determine adhesions between neighboring coils of intestine or between the bowel and other structures. They are also helpful in showing delayed emptying of the stomach in cases of duodenal stricture or obstructions to the entrance of the bismuth enema in cases of obstruction in the lower bowel. The administration of bismuth or barium by mouth is contraindicated in cases of acute obstruction with severe symptoms.

Urine.—The time of occurrence and the degree of indicanuria have been utilized as indications of the seat of obstruction. The amount of urine is sometimes significant. The higher the obstruction is situated in the small intestine the more intense will be the vomiting, and, consequently, the greater the loss of water from the system. At the same time, there is a failure of the absorption of liquid from the lower bowel. Therefore, an early reduction in the quantity of urine is significant of obstruction high up in the small intestine. In this type of obstruction the non-protein nitrogen of the urine may be increased and the chloride content decreased.

Obstruction Due to Foreign Bodies or Fecal Masses.—Among the causes included under this heading are gall-stones, intestinal calculi and parasites, various foreign bodies, and masses of fecal matter.

Gall-stones.—These are a rare cause of intestinal obstruction, as their size is only infrequently sufficiently large. They may, aside from direct obstruction, be the occasion of volvulus or of obstruction resulting from adhesions between the gall-bladder and some portion of the intestinal tract. The proportion of cases found by various authors ranges from 1 in 15 (Fitz) to 1 in 28 (Leichtenstern). The gall-stone usually finds its way into the intestine through a fistulous connection between the gall-bladder and the intestinal tract. Less commonly, it slowly works its way along the common duct, ulceration opening the way before, and cicatrization contracting the channel behind the calculus. After reaching the intestine, the stone may cause obstruction of the duodenum, or become impacted in the jejunum or ileum. The most common situation of lodgment is in the lower part of the ileum, near the ileocecal valve. In some cases the stone causes obstruction of the large intestine.

Symptoms.—The clinical manifestations may be divided into two stages: the first, in which active symptoms result from the escape of the calculus from the gall-bladder or the biliary passages into the bowel;

and the second, in which intestinal obstruction occurs. In the first stage, violent attacks of colicky pain attended with jaundice are characteristic. These may have been preceded by a history suggestive of biliary calculi. After entering the bowel, evidences of partial and temporary, followed by complete, occlusion may present themselves. As the stone usually finds its way first into the upper part of the small intestine, the symptoms, such as vomiting and colicky pain, are comparatively severe. After a little while these may be relieved, but they may be renewed with each successive lodgment in positions lower down, until finally a complete impaction occurs in the ileum, and signs of total obstruction appear. Even after complete impaction the calculus may be dislodged and the stone discharged from the bowel. In cases in which relief does not occur, death usually takes place between the fifth and the tenth day, but sometimes later. The outlook is always grave, as approximately one-half of the patients succumb.

Intestinal Concretions.—Intestinal concretions of sufficient size to produce obstruction are exceedingly infrequent. They consist of organic substances such as mucus, masses of bacteria, and fatty constituents impregnated with calcium and magnesium salts. Such concretions are usually formed in cases of enteritis, and the symptoms are therefore preceded by those of this condition. Gradually, as the foreign body enlarges, the attacks of colic, diarrhœa, and other evidences of enteritis become altered and give place to the evidences of more or less complete occlusion. In case of the formation of concretions in pouches of the bowel, especially of the large intestine, evidence of partial obstruction and a continuous intestinal irritation or colitis are encountered.

Foreign Bodies.—Foreign bodies other than those described are comparatively rare causes of occlusion. Fruit-stones, masses of intestinal parasites, hardened accumulations of mucus, balls of hair or vegetable fibre, and accumulations of medicinal substances, such as bismuth, salol, chalk and other insoluble substances taken by the mouth, may occur. Such obstructions are at first partial, and may continue so for a long time. Foreign bodies swallowed by hysterical or insane persons, or children, may cause obstruction. Hardened masses in the lower part of the large intestine may set up irritation and occasion a diarrhœa which confuses the diagnosis. More commonly, fecal matter accumulates above and around the foreign body until more or less total obstruction has resulted.

Obstruction Due to Bands.—Intestinal obstruction may result from the constriction of a portion of the bowel by a band or adhesion formed by a previous inflammatory condition, or by various abnormal bands of fibrous tissue that result from developmental conditions. In a similar manner a Meckel diverticulum may be the occasion of this form of occlusion. Subsequently a coil of intestine may become constricted by passing beneath or over such a band, and the distention of the portion of the coil beyond the band may prevent its escape.

A Meckel *diverticulum* is quite a frequent cause of obstruction, having been met with in 21 of 669 cases at the London Hospital. If the diverticulum remains connected with the umbilicus, the conditions are such that obstruction of a coil of intestine may readily be produced;

still more, when the free end of a diverticulum has formed a new attachment to the mesentery or some other part in the abdomen. A coil of bowel passing over or beneath the diverticulum may become twisted upon itself (volvulus), or may become variously knotted or contorted. Besides Meckel's diverticulum, bands may be formed by the attachment of the tip of the appendix to the appendices epiploicæ, the Fallopian tubes, or other structures within the abdomen, and strangulation of a loop of intestine may be the result. Occlusion by internal bands usually involves some part of the small intestine. The large bowel is relatively fixed and the lumen is such that strangulation beneath a band is infrequent. A coil of bowel may be held beneath a band for some time without symptoms. When, however, fecal accumulation or gaseous distention has increased its size, obstruction may occur and may rapidly increase from pressure upon the veins and consequent stasis.

Symptoms.—These are usually sudden and acute, and frequently follow after some strain or effort, or after acute digestive disorders with distention of the intestinal tube. The symptoms are those of acute obstruction from any cause, beginning with sudden pain and marked nausea and disturbance of the stomach. The evidences of obstruction follow rapidly, and the patient suffers early prostration and collapse. In many cases, however, the onset is less acute, and the symptoms are less violent. In these instances, pain and gastric disturbance may develop gradually and distention increases progressively. Evidence of more or less obstruction may be found, but the nature of the obstruction may be quite uncertain. When a coil of intestine is strangulated by a band, the occluded portion tends to undergo pronounced distention from the accumulation of gases and the retention of its contents; and a painful swelling may be felt through the abdominal walls. The distention may be so great that this is quite hard, and the percussion note over it may be relatively dull, from the tenseness of the walls.

Obstruction Due to Internal Hernia.—The term internal hernia is applied to hernial displacements of the intestines into the subperitoneal or retroperitoneal spaces without any protrusion externally. Among the *situations* in which they may occur are: (*a*) The subperitoneal tissue in the region of the inguinal rings, when the hernia may be associated with external hernia or independent of the latter. Not rarely such hernias have resulted from the reduction *en masse* of an external hernia. (*b*) Duodenojejunal hernia, a protrusion of part of the jejunum into the retroperitoneal tissues on the left side of the abdomen, beneath the crescentic fold of peritoneum, the plica duodenojejunalis. A number of such instances have been reported, and occasionally strangulation has occurred. (*c*) Pericecal herniæ, in which group are included hernias into the various pericecal or retrocecal pouches. (*d*) Intersigmoidal hernia, a form of considerable rarity, in which the hernial sac occupies the fossa occasioned by the sigmoid artery. (*e*) Herniæ of the foramen of Winslow, in which portions of the small intestines or, more rarely, of the large bowel extend through Winslow's foramen. (*f*) Herniæ into Douglas' pouch. (*g*) Herniæ projecting into the broad ligament of the uterus. (*h*) Diaphragmatic herniæ.

The last-named is the most frequent and most important form of internal hernia; about 1200 cases have been reported. A distinction is made between true and false diaphragmatic hernias, the former being cases in which the abdominal viscera extend through an opening in the diaphragm covered by a sac composed of peritoneum, pleura, or both. The false variety is that in which a free connection exists between the thoracic and the abdominal cavity (eventration). The latter variety is the more common. Diaphragmatic herniæ may be classified, also, as congenital or acquired, the latter being more frequent, and usually the result of traumatism causing rupture of the diaphragm. They are usually on the left side, and among the positions most commonly involved are the opening for the œsophagus and an area immediately behind the stomach. The stomach is most frequently displaced through the abnormal opening, next to which in point of frequency the colon, the omentum, or other parts of the intestinal tract may be involved. In exceptional cases the spleen, pancreas, or kidney is displaced into the thoracic cavity. Strangulation of the misplaced gut is a serious complication with a high operative mortality. Volvulus occasionally occurs.

Symptoms.—Sometimes these are wholly wanting and a diagnosis may be made by the signs indicating the presence in the pleural cavity of air-containing viscera, and the restriction of respiratory movements on that side. Displacement of the heart may be more or less conspicuous. Dyspnœa on lying down or after meals, dysphagia, intermittent tachycardia and thoracic discomfort may be present. The condition resembles most closely a pneumothorax, which, however, is usually distinguished by the fact that it commonly involves the whole pleural cavity, and is frequently right-sided. The auscultatory phenomena, especially the occurrence of amphoric breathing when a fistulous communication with the pleural sac exists, are quite distinctive. Difficulty in swallowing, vomiting, and other gastric symptoms, and sometimes intestinal obstruction, may occur in diaphragmatic herniæ, and are not met with in pneumothorax. Improvement in roentgenologic methods has greatly facilitated diagnosis, so that now the great majority of cases can be identified.

Obstruction Due to External Hernia.—The term external hernia is applied to hernial displacements of the intestines, through various openings, out of the true abdominal cavity. Such displacements include protrusions into or through the femoral and inguinal rings, the obturator and sciatic foramina, the umbilicus, perineum, and areas of weakness in the anterior abdominal wall (ventral or incisional hernias) or the lumbar region (Petit's triangle). *Incarceration* implies obstruction to the fecal current alone, in an irreducible hernia. It is most common in umbilical and inguinal hernias. The herniated bowel is hard, tender and painful, usually dull on percussion, diminishable in size by pressure, and transmits an impulse on coughing.

Strangulation implies interference with the circulation of the herniated bowel, usually but not always with obstruction of the fecal current. It is a much more serious condition than incarceration. It occurs oftenest in indirect inguinal, femoral, umbilical and incisional hernias. The affected bowel is tender and painful, the hernia is irreducible, and no impulse is transmitted on coughing.

The presence of incarcerated or strangulated hernia should be carefully excluded by examination in every case in which the symptoms are indicative of intestinal obstruction or other acute abdominal disease.

Obstruction by Incarceration of the Bowel in Slits or Holes.—An occasional cause of intestinal obstruction is the passage of a loop of the bowel through a hole or slit in the mesentery or omentum. The mesentery is the most frequent site of such imperfections and Treves has described a spot between the ileocolic and terminal mesenteric artery which is normally thin and readily becomes patulous. A gradual perforation of such a weak space may occur, but more commonly the perforation results from some violent injury that forces a portion of the bowel through the weakened area. Occasionally congenital holes are encountered. Sometimes, after inflammatory conditions, adhesions of the omentum and other structures may be so arranged that spaces are left between the adherent portions, and the bowel may be involved in these. The symptoms of obstruction due to this cause are similar to those of incarceration by bands of adhesions. They develop with great acuteness, and usually are violent in their manifestations.

Obstruction Due to Peritoneal Adhesions.—The adhesions that produce such constriction may result from any form of acute peritonitis or that associated with tuberculosis, cancer, etc. Similar adhesions may follow operations, particularly when drainage has been required.

Pathology.—The constriction may be annular, causing a limited contraction of the bowel similar to that due to stricture of the bowel, or a kinking or irregular contraction may be produced by looping over the bowel. In some cases the obstruction is due to a matting together of neighboring coils of intestine, or to close attachments to the parietal peritoneum by adhesions or by contraction of the mesentery. Annular adhesion or cicatricial formation in the peritoneum may result from ulceration within the bowel, or may follow peritonitis.

Kinking of the bowel without any distinct annular stenosis may occur under a variety of conditions, in which, following a localized peritonitis, short and firm adhesions have formed between the bowel wall and the abdominal parietes or one of the abdominal viscera. In many instances such kinks are multiple. In some cases, although adhesions occasion no sharp angulation, they may interfere sufficiently with peristalsis to result in partial obstruction.

Symptoms.—There may be no symptoms despite very extensive adhesions or deformations, and sometimes, even in cases in which almost universal agglutination is met with, very little interference with peristalsis is encountered. When obstruction occurs, the symptoms are those of gradually developing intestinal stenosis. As in other forms of organic obstruction, the symptoms may come on in a gradual manner, or may develop rather suddenly with attacks of pain, violent and visible peristalsis, and distention. Tumefaction may be found at the seat of obstruction, owing to the distention of coils of intestine adjacent to or included within the zone of adhesion.

Obstruction Due to Stricture of the Intestine.—By this term is meant a narrowing of the bowel by changes in its wall. This definition would

include all forms of new growths involving the bowel, as well as other disease processes affecting it. As here employed, it will be limited to cicatricial strictures which in the great majority of cases follow ulceration. Tumors and some other conditions causing narrowing of the lumen of the bowel (diverticula) will be discussed elsewhere. Of the various forms of intestinal ulceration those due to tuberculosis, stercoral accumulations, ulcer of the duodenum, dysentery, and syphilis are the ones that are prone to be followed by cicatricial strictures. Not rarely the strictures following tuberculosis are multiple. The hyperplastic form has been considered in a separate place. In this there may be marked encroachment upon the lumen of the bowel, just as in carcinoma or other tumors. In cicatricial ulceration of tuberculous nature, annular contractions occur without great thickening of the coats of the bowel. Strictures following *duodenal ulcer* have the same general characters as the constrictions of the stomach or its pylorus resulting from gastric ulceration. Jejunal ulcers may have the same termination.

Strictures following stercoral ulceration are met with in various parts of the large bowel, especially at the flexures, in the cecum, and in the rectum. An annular scar, with more or less thickening of the wall of the bowel, is usually found in such cases. It is not improbable that secondary carcinomatous change occasionally originates in such lesions. Strictures following syphilitic ulceration are most common in the rectum. Marked thickening, with irregular scar formation and constriction, characterize these cases. Strictures following *dysentery* were formerly regarded as very common. Woodward found not a single case of stricture in the 9431 fatal cases of dysentery occurring among the Union troops. A few instances have, however, been reported in the literature. Strictures following various traumatic injuries of the bowel, or after sloughing due to intussusception, hernia, etc., are occasionally met with.

Symptoms.—When a stricture occupies the small intestine, the symptoms may be relatively inconspicuous, owing to the fact that the intestinal contents in this portion of the bowel are normally fluid, and, therefore, unlikely to become stagnated. The occurrence of diarrhœa in some of these cases has been referred to in discussing the general symptomatology. A stricture in the large bowel much more readily produces obstruction by the gradual accumulation of hard fecal matter.

Diagnosis.—This offers greatest difficulty in cases of stricture of the large bowel, with hyperplasia of the intestinal walls. In such circumstances a differentiation from carcinoma may be very difficult. Roentgenologic examination may aid materially in the diagnosis.

Treatment.—This is purely surgical, unless the stricture is of small calibre or situated high up, when careful attention to the condition of the bowel may prevent difficulty.

Congenital Stenosis of the Intestine.—This is not uncommon and the great majority of cases occur at the ano-rectal junction. Leichtenstern found the proportion of cases as follows: 375 at the ano-rectal junction, 75 in the small intestine, and 10 in the colon.

Compression of the Bowel.—Intestinal obstruction is sometimes caused by the pressure on relatively fixed portions of the bowel by tumors,

displaced organs, etc. Frequently localized peritonitis, with the formation of adhesions, contributes largely to the obstruction. The rectum is the portion of the intestine most frequently compressed, 60 per cent. of Leichtenstern's cases having this location. Among the causes, fibroid tumors, carcinoma, and misplacements of the uterus are the most frequent, but abscesses, extra-uterine pregnancy, and other causes are also met with. Compression may also occur in other parts of the large intestine, or even in the small bowel. The *symptoms* are sometimes acute but in the majority of cases some evidence of chronic obstruction precedes the acute symptoms.

Intussusception.—Intussusception, or invagination, is a condition in which one portion of the bowel extends into a neighboring portion in such a manner that the former is ensheathed by the latter. The part of the bowel within the ensheathing portion is known as the *intussusceptum*, the outer portion as the *intussuscipiens*. On transverse section there will be found three thicknesses of bowel: (1) the outer, or ensheathing; (2) the returning part of the intussusceptum; and (3) the entering part. The term *neck* is applied to that portion of the intussusception where the intussusceptum passes within the ensheathing bowel. The doubling of the bowel where the intussuscipiens joins the returning layer of the intussusceptum is known as the *collar*. Occasionally an intussusception is incomplete, lateral, or partial when only a part of the circumference of the bowel is drawn into another part Usually the intussusceptum extends downward into an intussuscipiens, but ascending or retrograde intussusceptions sometimes occur. The term compound intussusception has been applied to cases in which a second intussusception extends into the first, so that a section would show five or more layers of bowel.

Etiology.—A distinction should be drawn between agonal intussusceptions and the pathological variety. In the former, which are multiple, violent peristaltic contractions doubtless play an important part. In pathological intussusception independent of the agonal period, the explanation is usually to be found in some organic defect which occasions a prolapse of a segment of the bowel into a portion beyond; or in some pathological lesion of a part of the bowel which is carried downward into a portion beyond. Thus if a direct prolapsus of a portion of the bowel into a segment beyond occurs, the prolapsed portion is seized by the peristaltic contractions of the part into which it extends, and is carried forward in the same manner as intestinal contents are usually transported. In the same way a polypoid or other tumor of the bowel, an inverted Meckel diverticulum or appendix, or some other pathological condition, may occasion the beginning of an intussusception. A prolapsus of the ileocecal valve is a common cause.

Various investigations of the etiology of intussusception in cases in which no antecedent pathological lesion of the bowel has been found have indicated that the primary condition is a spasm of the circular muscle of the bowel in some portion. This constricted area is grasped by the segment immediately below, and thus starts the process that

terminates in a complete invagination. A number of different developmental defects may predispose strongly to this condition, and may be the initial cause, as when there is an undue size of the large intestine as compared with the small and a consequent tendency to prolapsus. Abnormalities of the mesentery similarly predispose by permitting of the more ready invagination of one part of the bowel into another.

Immediate Causes.—The study of large series of cases of intussusception shows an absence of any definite immediate cause in half or even a larger proportion of the cases. In a relatively small number, some history of acute intestinal disturbance or of injuries is met with.

Age.—Intussusception is the most common form of intestinal obstruction in childhood and infancy. Among Leichtenstern's 593 cases, 131 occurred during the first year of life. In Weiss' 321 cases, 177 occurred during the first year. In the latter series, 85 occurred in the second to the fourteenth year, and 59 after that time.

The Location of Intussusception.—The agonal invaginations are usually found in the small intestines. Pathological intussusception may occupy any part of the intestinal tract, but much more commonly originates at the ileocecal valve than at any other point. In the majority of cases, especially in childhood, the ileocecal valve prolapses into the cecum and thus becomes the apex of the intussusceptum, dragging the ileum after it. The cecum and colon form the outer and middle layer, the ileum the inner. The term ileocecal intussusception is applied to such cases. Less frequently the ileum prolapses through the valve into the colon and is carried farther on. The name ileocolic is given to this form, which is certainly rare. Leichtenstern found, in an analysis of cases at all ages, that invagination of the small into the large bowel occurred in 52 per cent., ileac intussusception in 30 per cent., and colic in 18 per cent. In adults the ileac and the ileocecal varieties were of approximately equal frequency. Other large series have shown about similar proportions; but in small groups of cases great variations have been encountered.

Pathology.—Secondary changes take place in the intussuception, according to the degree of constriction at the neck. There is practically always more or less interruption of the circulation in the mesentery entering into the invagination, and a consequent intense congestion of the intussusceptum. This becomes dark red, purplish, or blackish, and is swollen as the result of the hyperemia and attendant œdema. Ecchymotic hemorrhages occur within the bowel wall, and exudation of hemorrhagic fluid into the lumen of the bowel takes place. The most marked change occurs in the middle layer of the invagination.

In the later stages, when the swelling of the invaginated portion has become extreme, complete obstruction of the lumen of the bowel occurs, and at the same time an increase of circulatory interference with resulting gangrene. In acute cases this may develop as early as the end of the first day; although it is usually not met with, even in the acute cases, before the expiration of three or four days. In the chronic cases gangrenous changes may be delayed for a long time, sometimes not appearing until a number of months after the onset. The gangrene usually first

affects the apex of the intussusception, but in other instances it begins at the neck. As the result of the gangrenous necrosis, portions of sloughed-off bowel may be passed from the rectum.

Peritonitis affecting the enfolded portion of the serous covering of the bowel (that is, the serous coat of the innermost and middle reflection of the bowel, where they lie in contact) sets in rather promptly; usually becoming marked by the end of the second or third day. This may be confined to the region of the neck of the invagination, or may be extensive, and involve the entire serous coating within the sac. The invaginated portions become agglutinated, and reduction of the intussusception is more difficult. In the late stages, especially in the chronic cases, firm adhesions may form between the two layers of peritoneum adjacent to one another. When such adhesions have formed at the neck of the sac, and the intussusceptum has been discharged after sloughing or gangrene, relief may occur. More commonly a stenosis of the bowel results from cicatrization, and a partial intestinal obstruction, which later may become complete, is the terminal condition.

Symptoms.—The symptomatology varies widely, some cases being comparatively slow in development and chronic in course, and others highly acute in onset and terminating rapidly. In the great majority the onset is sudden and occurs without any apparent predisposing condition. Sudden violent pain of a cramp-like character usually initiates the disease, and is speedily followed by nausea and vomiting. In many instances tenesmus and one or more movements of the bowels follow, and sometimes a diarrhœal condition sets in. The movements may be composed of mucus alone, of mucus mixed with blood or of pure blood. The degree of tenesmus and of diarrhœa depends to some extent upon the situation of the intussusception, being more marked when this involves the lower portion of the bowel or the rectum.

Distention of the abdomen may appear, but is not, as a rule, a marked condition. Direct physical examination discloses a palpable tumor in many cases. This is usually felt in the left side of the abdomen, when the intussusception has become extensive and has reached that point. The tumor may, however, be felt at the ileocecal region, where the intussusception, as a rule, begins. It is usually elongated, cylindrical, or sausage-shaped. Contractions of the bowel ensheathing the invaginated portion may cause a change in the consistency as well as in the size of the mass. Occasionally an intussusception extends so far as to protrude through the anus. In chronic or slowly developing cases the tumor may be found to change its position, moving in the direction of the intestinal tract.

In the acute cases, after an onset of this character, symptoms of depression and collapse occur, usually within from one to three days. At the same time the vomiting, as in other cases of intestinal obstruction, becomes fecal in character. In chronic cases, if the onset has been acute, the symptoms gradually subside and may become relatively inconspicuous. In other cases, the clinical course is of a chronic character.

The most important symptoms are the pain, the tumor, and the

peculiar behavior of the bowels. The *pain* in the early stages may be intense—so severe, indeed, that it occasions collapse. This is particularly marked in the acute forms in early childhood. Later, paroxysms of colicky pain recur from time to time, with more or less frequency. Attending this there may be a tonic contraction or stiffening of the segment of the intestine above the point of intussusception, and in other cases of intestinal obstruction. *Tenesmus* is more frequently met with in this form of intestinal obstruction than in any other; it is earlier in its appearance, and more intense the nearer the invagination approaches the rectum. The character of the stools is a highly important diagnostic indication. There may at first be a discharge of fecal matter from the lower bowel, but soon the movements, if they continue, become mucous, bloody, or of mixed mucus and blood, while the discharge of fecal matter ceases. The evacuations may be attended with sharp recurrences of the characteristic tenesmus. Sometimes large hemorrhagic movements or actual hemorrhages may occur.

Prognosis.—The termination of intussusception varies greatly. A rapid course with a fatal termination is more frequent in infants than in the intussusception of later life. Subacute and chronic cases, running a course of weeks or even months, occur as a rule in the older subjects. Even in these, however, the eventual termination is usually fatal. Reference has been made to occasional spontaneous cures; but, taking the number of these in large series, this outcome is exceedingly rare. Occasionally complete cure by spontaneous or induced disinvagination may take place in cases in which peritonitis and adhesions have not developed or have been so slight that the invaginated portion was able to escape. In a few instances such relief occurred after the condition had persisted for a considerable time.

Treatment.—In cases of intussusception recognized early, and especially in infants, manipulation combined with enemata may effect relief in a considerable proportion of instances. The mass is grasped in the fingers of one hand (the patient being anesthetized) and gentle traction made with the other hand in a direction to effect disinvagination, or pressure is made against the apex of the invagination to cause its release. Following this, or between the efforts of manual relief, enemata of water (from $\frac{1}{2}$ liter in children to 2 liters in adults) may be allowed to flow into the rectum through a soft rubber tube and under a pressure of four or five feet, great care being taken to lower the funnel should undue distention seem to occur in the lower bowel. In adults these methods of treatment are less often satisfactory. In them as well as in infants, if the simpler plan of treatment has failed, surgical treatment must be adopted before too long a time has elapsed.

Volvulus.—This term is applied to various kinds of twisting, knotting, or rotation of segments of bowel, resulting in partial or complete obstruction. A loop of intestine may become obstructed by rotating about its mesenteric attachment, which acts as a sort of pedicle; in other cases volvulus is due to a twisting or rotation of the bowel on its own longitudinal axis, while in still other cases one loop of intestine twines about

the mesenteric attachment of another, or intertwining may take place between two or several coils.

Etiology.—Abnormal length of the mesenteric attachment of a loop of bowel, especially when combined with a lateral contraction of the mesentery, is the most important cause of volvulus. The mesentery may be elongated congenitally or it may become stretched as a result of continued constipation and overloading of the affected portion of the bowel, and some stretching may result from adhesions of some part of the intestinal canal to fixed abdominal structures. A not uncommon cause of elongation is the inclusion of a coil of intestine in a hernial sac. Narrowing or contraction of the mesentery may occur without special elongation as a result of inflammatory conditions. A laxness and relative elongation of the mesentery may be caused by a loss of fat in the abdominal walls and in the mesentery itself. In women, after repeated pregnancy, these conditions frequently occur.

The conditions which predispose to volvulus are more frequently found in persons of advanced years than in the young, and volvulus is therefore most common in the aged or those past middle life. The immediate cause may be a strain or some effort, as in lifting, or a traumatism, such as in compression of the body. Sometimes overloading of the intestinal tract combined with some effort or strain is of importance. Thus in old people who have suffered from habitual constipation the sigmoid flexure becomes elongated and its mesentery stretched.

Pathology.—In simple volvulus, a loop of intestine twists about its mesenteric attachment. There may be a partial turn or several complete turns. In the former case the obstruction of the bowel is partial or incomplete; in the latter it is almost certainly complete, and in addition the bloodvessels become so compressed that intense venous engorgement results. Whether the obstruction is partial or complete, but especially in the latter case, distention of the obstructed portion of the bowel rapidly ensues. The bowel becomes dark red or purplish in color, and its walls are deeply engorged with blood and swollen by œdema. Then extravasations of blood are seen upon the surface and blood-stained liquid exudes into the lumen of the bowel as well as into the peritoneal cavity. Finally gangrene takes place. The striæ of the bowel are obliterated by the overextension, and rents of the serous coat may occur. Rupture of the bowel, however, rarely takes place. It is more likely to be found above the volvulus than in the affected portion.

Peritonitis sets in rather promptly as a result of the escape of bacteria through the injured, congested, and œdematous walls of the bowel. When bloody extravasation is present in the peritoneal cavity the escaping bacteria may occasion putrefactive changes.

Seats.—Volvulus most frequently involves the sigmoid flexure, but may occur at the junction of the small and large intestine or in some portion of the small intestine. In volvulus of the sigmoid there is usually a simple rotation of the flexure about its mesenteric attachment. The rotation is usually in such a direction that the rectum is carried posteriorly to the descending colon, but sometimes the twist is in the opposite direction, so that the rectum is carried forward and lies in front. Occasionally

the sigmoid may become coiled about a loop of the small intestine or about the pedicle of a pelvic or abdominal tumor.

Volvulus at the junction of the small and large intestine usually involves both the ileum and colon and is occasioned by an abnormal length of mesentery. Simple rotation of the colon on its own axis has been described, but is probably rare.

Volvulus of the small intestine resembles that of the sigmoid. Rarely two or more loops may be intertwined. Unusual length of the mesentery is the ordinary cause; but some other pathological condition, such as the passage of a loop of the bowel through an internal hernial orifice or under a band, may be the direct cause of the volvulus. In these conditions the loop of bowel after incarceration becomes twisted upon itself at the point where it is engaged in the hernial opening or under a band. A foreign body within the bowel may occasion the twist.

Symptoms.—These are usually those of an acute intestinal obstruction. When the obstruction is only partial in the beginning, there may be a subacute onset which goes on to complete obstruction as the volvulus increases. The symptoms vary according to the location of the lesion. In volvulus of the sigmoid there is usually sudden severe pain followed by paroxysms of cramp or colic, and, as a rule, by absolute constipation. Reflex disturbances, such as vomiting, are often wanting because of the low situation of the obstruction. Sometimes, instead of constipation, there is a tendency to mucous discharges with tenesmus, and occasionally ordinary diarrhœa may occur. The abdomen soon becomes intensely tender and enormously distended. The superaddition of peritonitis, which usually occurs within twenty-four to forty-eight hours, causes increased tenderness and swelling and adds greatly to the prostration.

In volvulus affecting other portions of the intestine the symptoms are similar; vomiting is more conspicuous, especially in cases in which the small intestine is involved in its upper portions. In all cases the distention of the coil of the bowel included in the volvulus causes a localized tumefaction, which may be so hard that it simulates a solid mass. The situation of this may indicate the location of the volvulus, although it must be remembered that the length and mobility of a cecum and even of the sigmoid may readily cause confusion.

Prognosis.—This is usually very grave. In some instances the condition relieves itself spontaneously. This is probably more common in the case of the small intestine, but certainly occurs even when the sigmoid is involved. Usually, unless speedily relieved by surgical means, localized peritonitis and gangrene of the involved area soon take place, and death speedily follows.

Differential Diagnosis of the Conditions Causing Obstruction.—It is often impossible to distinguish between the different causes of acute or chronic obstruction, although sometimes antecedent conditions, the manner of development of the symptoms, and the clinical course may furnish fairly reliable evidence of the nature of the condition.

Strangulated or incarcerated *external hernia* is usually readily demonstrable as a visible or palpable protrusion, tender and painful, often transmitting an impulse when the patient coughs, and incapable of reduc-

tion. Often an antecedent history of hernia can be obtained. Sometimes the protruding knuckle of gut may be very small, as in many femoral hernias, and difficult to demonstrate.

Among *foreign bodies* the most common cause of obstruction is gall-stones. When a biliary calculus enters the duodenum and causes obstruction, the vomiting and prostration at once reach grades of the highest severity. Relief may follow the dislodgment of the stone and its transportation to lower levels but if it remains high up, early fecal vomiting and collapse usually result. A preceding history of gall-stones and jaundice or other significant symptoms may make the diagnosis fairly certain.

Obstruction by *bands* usually involves some portion of the small intestine and causes symptoms of a decidedly acute character, with early development of fecal vomiting, prostration, etc. Internal hernia also involves the small intestine, and cannot usually be distinguished with accuracy from the former.

Intussusception usually involves the ileum or the ileum and cecum, and is more frequently found in childhood or early life than at or after maturity. The symptoms of onset are decidedly less acute than in obstruction of the small bowel by bands. Localization of the place of obstruction is sometimes readily made by the situation of the pain, the development of a local tumefaction, and the situation of stiffening or tonic contraction of the bowel. The localization of the obstruction, the discovery of a sausage-shaped tumor, the characteristic stools, and especially the occurrence in childhood may establish the diagnosis. In acute cases, however, especially those occurring in young infants, the intense pain and sudden collapse may mask other indications, and the nature of the condition may be difficult to determine.

Volvulus usually involves the sigmoid flexure, and occurs in persons of somewhat advanced years, and especially in the aged. The symptoms are slow in development and often inconspicuous until a late stage in the disease. The localization of the point of obstruction may often be established, although sometimes a redundant sigmoid may occasion confusion. Strictures and partial obstructions of the bowel may be suggested by the occasional occurrence of attacks of abdominal distention, with relief after active movements of flatus.

Obstruction by carcinoma and other tumors usually occurs in the large bowel. Although tumors in their general relations are considered elsewhere, some of the features that indicate a neoplasm as the cause of intestinal obstruction may be appropriately referred to in this place. Attacks of distention with active peristalsis and movements of flatus may occur from time to time, followed by more severe seizures, marked by violent abdominal colic. In these cases the patient himself may be able to recognize the point of obstruction by feeling the place of spasmodic contraction above the lesion. On palpation the physician may discover a hardening which appears at a certain place, and after a moment or two or a longer period of time relaxes. When the growth is situated favorably for palpation, or has reached considerable size, it may be discovered on abdominal palpation. When situated in the rectum, a digital rectal examination or the enteroscope may disclose its presence.

As in other forms of obstruction involving the large bowel, the passage of stools of characteristic form some time before complete obstruction has developed and the occurrence of mucous, mucopurulent and blood-streaked or bloody passages may aid. Bloody and mucous movements are more frequent in carcinomatous obstruction than in any other form.

Obstructions due to *fecal accumulation* rarely occur independently of other causes of obstruction, except when the accumulation takes place in the rectum as the result of habitual constipation. In these cases the development of the condition is so gradual that the existence of obstruction may not manifest itself until, more or less suddenly, paralysis takes place. In the earlier stages the most characteristic indication is the increasing difficulty of securing evacuations and the insufficiency of these. With this there may be a gradual increase in abdominal girth from general meteorism; and the colon throughout its length may be found distended beyond normal dimensions. Hardened masses may also be discovered in the left iliac region, or in the rectum. If the abdominal walls are thin and the peristalsis maintains itself actively, visible peristalsis may be seen for some time before the degree of contractions and the grade of obstruction cause sharp attacks of colic. In many instances of gradually developing impaction, fairly regular movements, seemingly adequate in quantity, may occur for some time after the onset. Still more puzzling are the cases in which a continuous diarrhœa results from catarrhal inflammation of the bowel by retained fecal masses. A similar condition occurs in some instances of carcinoma of the lower bowel.

Prognosis.—The termination of intestinal obstruction depends upon the nature of the obstruction and its completeness. In acute occlusions that cannot be relieved death may occur within a few hours, or not until several or many days have elapsed. Leichtenstern estimates the average duration at six days. Partial or chronic obstructions may persist for very long periods of time; in some cases for years. Repeated vomiting, excessive shock, prostration, and collapse are the usual conditions that precede death in acute cases; the persistence of such conditions is, therefore, a prognostic indication of great gravity. Another cause of death in acute cases is peritonitis. In cases of greater duration, toxemic manifestations usually set in before death ensues.

Recovery from intestinal obstruction may occur spontaneously in cases of fecal impaction or compression of the bowel; and sometimes in cases in which the obstruction is due to adhesions, bands, internal hernia, or the presence of foreign bodies within the bowel. In intussusception, spontaneous disinvagination may occur, or the intussusceptum may slough off and recovery may take place; while in volvulus the twisted loop of bowel may be spontaneously restored to its normal condition. A recurrence of obstruction after a primary relief sometimes takes place.

Treatment.—Practically all forms of intestinal obstruction demand surgical treatment. In cases of partial obstruction, however, and in some conditions like impaction of feces or the presence of foreign bodies within the bowel, medical treatment deserves a careful trial. In the early stages, before an absolute diagnosis of obstruction has been made and before surgical intervention can properly be advised, certain indica-

tions must be met by medical means. In cases, however, in which it has been thought well to institute medical treatment, this form of management should not be persisted in longer than a day or two, if relief of the obstruction is not apparent. It is far better to err on the side of too early operation than the reverse; and in all cases of doubt, surgical rather than medical measures should be adopted. Gentle manipulative attempts at reduction of external hernia may be made before surgery is employed, but care should be exercised not to injure the bowel.

In the beginning the patient should be placed at as complete rest as possible, and the diet should be restricted or completely withheld even if marked gastric disturbances are not present. Small particles of ice may be allowed to quench thirst; but the unrestricted use of ice may occasion disturbance of the stomach and is objectionable. Enemata of water and hypodermic injections of saline solutions may be given.

The use of laxatives must be condemned, except in certain special conditions. If they are effective at all in stimulating peristalsis, they will increase, instead of relieve, the abnormal conditions. Fortunately, when administered in error of diagnosis, vomiting usually causes their prompt expulsion. In fecal impaction purgatives are often desirable, although they must be employed with caution. Small doses of calomel or salines are preferable to more active remedies, because they produce serous outpourings without stimulating violent peristalsis. In cases of partial occlusion the accumulation of feces may be prevented by the occasional use of the same or other laxative remedies.

Enemata and colonic flushings are specially advisable in cases of obstruction due to fecal impaction. The repeated use of warm water, saline solutions, or oil may break up an impaction that threatens to cause complete obstruction. The injections must be given cautiously and without undue force, as they may stimulate violent peristalsis above the obstruction. The same plan of treatment is sometimes effectual in dislodging a foreign body; but the use of forced injections of fluids in cases of intussusception, volvulus, etc., cannot be too strongly condemned. Formerly inflation of the bowel with atmospheric air or various gases was practised for the relief of intussusception and other kinds of organic obstruction. This method also merits condemnation.

Opium and atropine are administered with advantage in some cases of obstruction for the purpose of quieting spasm or excessive peristaltic efforts. Thus in cases of internal hernia or occlusion by bands the obstruction may become more complete as the result of the violent peristalsis stimulated at the point of occlusion. Complete rest, the use of poultices or other warm applications, and small doses of opium or atropine, may relieve active peristalsis; and a release of the incarcerated bowel may take place, although this can rarely be hoped for. Similarly in cases of obstruction by foreign bodies the same remedies, especially atropine, may aid in relaxing spasm and thus facilitate the passage of the occluding body. Besides these indications, opium or morphine is sometimes necessary, even though operation is decided on to control the pain. The doses should be no greater than are required to allay suffering; and, generally speaking, hypodermic injections are preferable to administration by the mouth or by the rectum.

External treatment to the abdomen may be useful in cases of obstruction which can be relieved, such as those due to foreign bodies or impaction, and some cases of incarceration by bands, through slits, etc. Large poultices or warm fomentations may be used and, even though ineffectual in accomplishing a relief of the obstruction, they frequently give comfort. Massage of the abdomen is particularly helpful in cases of partial obstruction, such as are caused by adhesions after operations, or those due to the presence of foreign bodies. After relief from impaction in cases of narrowing of the lumen of the bowel, subsequent accumulations may be prevented by systematic manipulations combined with the administration of laxatives and the injection of warm saline solution or oil into the bowel. In acute obstruction, external manipulations must be used with the greatest caution.

In treating the toxemia of acute obstruction, the use of salt solution has been advised. This should be given intravenously or by hypodermoclysis. Haden and Orr recommend the use of larger amounts of NaCl than can be given in normal saline, and mention gr. xv (gm. 1) per kilo of body weight as an initial dosage.

Certain symptoms may require treatment before or after operation has been decided on. Among these, gastric disturbances are most important. Nausea and vomiting may greatly complicate the difficulties under which the patient labors and contribute largely to prostration. When laxatives are permissible, small doses of calomel may have a controlling effect. When the disturbance of the stomach is more intense, lavage is advisable. If resorted to early, this may reduce subsequent difficulties materially. Sometimes an actual cure of obstruction has been obtained from gastric lavage, as Kussmaul, first pointed out. Surgeons quite uniformly recommend lavage as being useful in allaying the danger from subsequent anesthesia, when vomited material so readily gains access to the lungs. If used at all, lavage should be resorted to early.

Surgical Treatment.—In all cases of obstruction in which the symptoms are not relieved within forty-eight hours under general and medical management, surgical intervention must be advised, and in many cases immediate operation should be recommended. Attempts to relieve volvulus and complete obstructions by bands and the like by means other than surgical operation are inadvisable, although occasional cures have been obtained from such treatment. In the long run, the loss of time and strength thus occasioned makes the subsequent operative measures less likely to prove successful.

VOLVULUS OF THE OMENTUM

Volvulus of the omentum may be considered briefly in this place on account of the resemblance of the symptoms to those of intestinal obstruction. The great omentum may become twisted in the same manner as a coil of intestine. This usually takes place either in a part of the omentum included in a hernia or in a contracted portion that had been contained in a hernia and afterward restored to the abdominal cavity. Sometimes the twisting is the result of adhesions of the omentum

to fixed structures. Occasionally several turns are observed, and some of these may be manifestly of considerable duration.

The omentum becomes swollen. œdematous, engorged with blood, and finally may undergo necrotic change from stasis. Hemorrhagic extravasations into its tissues and free exudation or extravasation into the abdominal cavity may take place.

Symptoms.—These are similar to those of intestinal obstruction. Sudden and severe abdominal pain with nausea and vomiting are the initial manifestations. The appearance of an abdominal mass, more or less tender on pressure, or the sudden distention of a hernial sac, if the twisted omentum is contained within the sac, are usually met with. Constipation is usually present but is less obstinate than in cases of volvulus of the bowel.

Treatment is purely surgical.

INTESTINAL OBSTRUCTION DUE TO MOTOR PARALYSIS

Partial or complete obstruction may be due to motor insufficiency or complete paralysis of the motor power of the bowel. Sometimes this results from direct or reflex causes without organic lesions affecting the bowel itself. More frequently such obstruction from paralysis is a concomitant of organic diseases of the bowel.

Functional Paralysis.—A complete paralytic obstruction has occasionally been observed as the result of injuries or diseased conditions, such as contusion, compression, or torsion of the ovary or testicle, various inflammatory conditions in the inguinal region or in hernial sacs, after operations for hemorrhoids, or in consequence of the passage of renal or biliary calculi. In such cases the paralysis of the bowel is a result of violent irritation of the sensory nervous mechanisms.

Cases have been observed in which the condition has followed paracentesis of large abdominal effusions or injuries to the abdominal cavity of various sorts, not involving the viscera. Similarly, after abdominal operations in which the intestines have not been involved, and in which there has been no peritonitis, partial paralytic conditions of the bowel are very frequent.

After the reduction of hernias, paralysis of the affected coils may occur, although the bowel presents no evidence of inflammatory or other organic change. In cases of intestinal obstruction involving the upper part of the small intestine, complete cessation of all movements indicates a secondary paralytic condition of the lower bowel. In all these cases there is a functional paralysis which may be explained by a direct or reflex stimulation of the inhibitory nerve, the splanchnic, which occasions cessation of peristaltic movements.

In another group of cases the paralytic condition is probably due to toxic conditions affecting the intestinal walls or the nervous mechanism of peristalsis. In this group may be included the occasional cases of paralysis of the bowel occurring in the course of severe attacks of pleurisy or pneumonia. Mannaberg and the writer have observed instances of this sort. In some cases the obstruction was so severe as to call

for operation. A similar condition occasionally attends cases of cholera, typhoid fever, and severe intestinal intoxications or enteritis. In all these instances the action of toxins upon the muscles or the nervous apparatus may explain the condition.

Paralysis of the Bowel Attending Organic Disease.—Much more common are the cases in which segments or a large part of the intestinal canal become obstructed by paralysis that is secondary to some form of intense organic disease. The more frequent and important cause of such paralysis is acute *peritonitis*. In cases of general peritonitis the bowel soon becomes quiescent; finally, all peristalsis ceases and a paralytic condition ensues. In localized peritonitis, such as that attending appendicitis, localized segments are involved. In chronic peritonitis and tuberculous peritonitis, obstruction of the bowel is more commonly due to adhesions or mechanical obstructions, although the inflammation of the bowel wall and the reflex nervous influences also play a part in the process. Embolism and thrombosis of the mesenteric vessels occasion a paralysis and consequent obstruction. In all those cases in which paralysis has followed organic lesions the cause of the motor palsy is in part the direct involvement of the wall of the intestine in the disease process, and in part the effect upon the nervous apparatus.

Occasionally paralysis is due to excessive accumulations of intestinal gases or of feces. In chronic constipation or partial obstruction of the bowel, or in various diseases in which a partial but not a complete paralysis has occurred, excessive meteorism may determine a complete paralysis; or the gradual accumulation of feces may so distend the bowel as to cause the complete cessation of peristalsis.

Symptoms.—The symptoms are practically those of obstruction by mechanical causes. When due to violent reflex nervous stimuli, as in cases of injury to the ovary or testicle, or to the passage of calculi, the onset may be attended with sudden intense pain, vomiting, and prostration, following which obstinate constipation and distention of the abdomen make their appearance. Although vomiting is usually marked, it less commonly becomes fecal than in mechanical obstruction. On auscultation peristaltic sounds are much diminished or entirely absent. This differs from the early stages of mechanical obstruction, when peristalsis is usually much exaggerated. Other symptoms may indicate the cause of the paralytic condition, and establish a correct diagnosis, although this is usually difficult. The course depends upon the cause. When some injury has occasioned the paralysis, a return to normal conditions may occur after the original disease has subsided.

Treatment.—This must always be directed to the original cause of the intestinal condition. Sometimes this may be controlled by medical means, as in toxic or inflammatory conditions of the bowels; in other cases, as when an injury has been sustained, local applications or cold or other local measures may be employed with advantage. Surgical intervention is frequently necessary. Moderate paralytic conditions of the bowel may sometimes be corrected by hypodermic injections of sulphate of eserin (gr. $\frac{1}{100}$ to gr. $\frac{1}{30}$) or pituitary extracts; by colonic douches of cool water or saline solution, or enemata containing stimulat-

ing remedies like asafœtida and turpentine. External applications, such as mustard plasters and turpentine stupes, may also be beneficial. In cases of paralysis of the bowel following other abdominal diseases, surgical treatment of the original condition alone can be relied upon.

INTESTINAL DIVERTICULA

Intestinal diverticula are classified as congenital and acquired. According to their anatomical peculiarities they can be divided into true and false diverticula. *True* diverticula are those composed of all the coats of the normal intestinal wall. *False* diverticula are those composed of only the mucosa and serosa. They are, in other words, hernial protrusions of the mucosa through defects in the muscularis. As most congenital diverticula are true and most acquired are false, the terms "congenital" and "true" and "acquired" and "false" have often been employed synonymously. Although in the majority of cases this holds good, some cases of the acquired form have apparently been true diverticula, so that the synonymous use of the terms "acquired" and "false" is not to be recommended.

Congenital Diverticula.—Meckel's diverticulum, so called, is the only form of congenital diverticulum that requires description as other forms are of extreme rarity. Meckel's diverticulum results from the persistence of the omphalomesenteric duct. This should be entirely obliterated by the sixth or seventh week of fetal life, but some remains of it are frequently found. It is apparently more common in males than in females. Kelynack found 4 cases of Meckel's diverticulum in 298 autopsies, all in males, while in 337 cases Rolleston found 10 instances, 9 of which were in males. The diverticulum usually takes its origin from the convex side of the small intestine, about 1 meter above the ileocecal valve. Exceptionally it arises from the upper portion of the small intestine. It varies from 3 to 10 cm. in length and may be as long as 25 cm. The wall of the diverticulum is commonly composed of the same structures as the intestinal wall. The lumen of the intestinal end of the diverticulum is large, frequently as large as that of the intestine itself. A valve-like fold of the mucous membrane at times occludes the opening of the diverticulum. Toward the free end of the diverticulum the lumen decreases, so that the process has something of a conical form. Occasionally the end is enlarged, at times assuming a hammer-like form. In unusual cases the same lumen is maintained throughout the entire extent of the diverticulum.

Usually the end lies free within the abdominal cavity. Occasionally, however, it remains attached to the umbilicus. Under these circumstances the lumen of the peripheral end alone becomes obliterated, forming a fibrous cord, but in other cases the entire duct may remain patulous, thus forming a free communication between the external surface and the ileum, permitting the discharge of intestinal contents at the umbilicus. Hubbard has collected 9 such cases, in all of which operation resulted in a cure. The remains of the duct in the umbilicus may give rise to an adenomatous growth or carcinoma.

When, as is usually the case, the peripheral portion of the lumen becomes obliterated, the fibrous cord resulting may remain attached to the umbilicus and later become the possible cause of intestinal strangulation, or this cord may atrophy, and the end of the diverticulum then becomes free within the abdominal cavity. Subsequently inflammatory conditions may cause the free end to become adherent to any point within the abdominal cavity with which it may come in contact. This is most frequently the mesentery. Cazin and Halstead[1] have made exhaustive analyses of the various places and structures to which the peripheral end of Meckel's diverticulum may attach itself, and Fitz[2] discussed the possibilities of strangulation of portions of the intestinal tract by such adherent diverticula.

If, finally, the diverticulum assumes its most frequent form, a finger-like projection, the tip of which lies free within the abdominal cavity, it may remain an entirely harmless appendage. On the other hand, it may be the seat of various phenomena of extreme gravity. It may be the seat of a volvulus by rotating upon its own axis; it may be the starting-point of an intussusception by becoming inverted into the ileum; or it may become knotted about a coil of intestines and produce stricture. It may be the seat of an acute inflammatory process. If the diverticulum possesses its own mesentery, this may produce a stricture of the ileum. Occasionally the lumen becomes occluded at its intestinal end, inducing cyst formation which may suppurate or by pressure produce obstruction. Ulcerations of the mucosa of the diverticulum, sometimes perforative, may result from fecal accumulations or from typhoid or tuberculous infection.

Acquired Diverticula.—These may be true or false. True acquired diverticula are of extreme rarity. They are usually in the form of minute spherical or conical traction diverticula, occurring as a result of adhesions due to some extra-intestinal inflammatory condition. It appears possible, however, to have a true acquired diverticulum which is not the result of traction. Such a condition appears to have been present in the first case reported by Mayo, Wilson, and Giffin.[3] False diverticula are hernial protrusions of the mucous coat through the muscular coat. As the protrusion of the mucous coat makes its way through the muscular coat it naturally carries the serosa with it, so that usually the wall of the diverticulum is composed of mucosa and serosa. At times a few muscular fibres are found between the two layers. These diverticula may be conical, cylindrical, hemispherical, or irregularly lobulated, and vary in size from that of a pea to that of an apple. They may occur throughout the entire intestinal tract, but are more frequent in the large intestine. As a rule, they are multiple, and at times occur in extraordinary numbers; Hansemann recorded 400 in a case. They differ from Meckel's diverticulum in that they usually arise from the concave side of the intestine close to the mesenteric attachment. At times they occur between the peritoneal coats of the mesentery. It has been claimed that the simple

[1] Halstead, *Annals of Surgery*, 1902, **35**, 471.
[2] *Amer. Jour. Med. Sci.*, 1884, **88**, 30.
[3] *Transactions of the American Surgical Association*, 1907, p. 240.

intra-intestinal pressure resulting from long-continued constipation is the etiological factor. Another view is that they result from the atrophy of some of the fibrous elements of the intestinal wall. A view that has many adherents is that advanced by Klebs, namely, that the point of entrance of the mesenteric vessels into the intestinal wall forms a focus of lessened resistance through which the mucosa forces itself, carrying with it the overlying serosa. The primary factor is decreased resistance of the intestinal wall. This may be due to structural weakness at the points of entrance of the vessels or to areas of atrophy of the fibrous or muscular tissues of the bowel wall. The various theories of the production of intestinal diverticula were thoroughly discussed by Fischer.[1]

According to Gordinier and Sampson, acquired diverticula were found 64 times in 8132 autopsies (Dresden Hospital); 19 times in 2600 autopsies (Johns Hopkins Hospital); twice in 953 autopsies (Bender Hygienic Laboratory); once in 2382 autopsies (Boston City Hospital). Careful investigation of left-sided tumors will doubtless reveal more.

Retention of fecal matter and infection may occasion inflammatory lesions of the mucous lining or entire wall of the diverticulum and localized peritonitis, sometimes with considerable induration, may surround the diverticulum and involve the adjacent portions of the bowel wall. Tumors of considerable size and easily palpated through the abdominal wall may result. In cases of inflammation confined to the mucosa, ulceration and perforation into the peritoneal cavity may occur, sometimes quite acutely. In the case of the tumor-like indurations surrounding the diverticulum intestinal obstruction is more frequently the consequence. The term "diverticulitis" may be applied to both classes.

A variety of diverticula requiring special mention are those occurring in the duodenum at the site of the papilla of Vater. They are apparently due to weakening of the intestinal wall at the point of entrance of the bile-duct. Keith claims that they occur in women from a forced visceroptosis, as the result of the pressure of corsets. The forced descent of the duodenum is not participated in by the bile or pancreatic ducts, on account of their more fibrous consistency, and a pouching of the intestinal wall in the neighborhood of the papilla thus results.

Bland-Sutton[2] describes a form of abscess of the epiploic appendages caused by the penetration of foreign bodies through the intestinal wall and their lodgment in the epiploic appendage. Very often after middle life there appear in the wall of the gut, especially of the descending colon, small pouch-like diverticula in which small foreign bodies may lodge and so penetrate the intestinal wall. In thin individuals the foreign body would probably enter the peritoneal cavity, while in the more obese it might enter the epiploic appendages and set up inflammation.

In a large majority of cases acquired diverticula give no clinical evidence of their existence. Lately, however, those situated in the descending colon, and especially in the sigmoid flexure, have been shown to be the cause of very profound diseased conditions, and their recognition explains some obscure phenomena having their seat in the left iliac

[1] *Jour. Exper. Med.*, 1901, **5**, 333.
[2] *The Lancet*, 1903, ii, 1148.

fossa. Among the contributions which have shed light upon the condition are those of Mayo, Wilson, and Griffin, Brewer,[1] and Beer.[2]

The *clinical features* presented by these cases may conveniently be divided into the inflammatory and the obstructive.

The *inflammatory* phenomena may be the result of either a virulent infection of the diverticulum or perforation. The symptoms may briefly be described as those of appendicitis on the left side. The patients are usually males over forty-five years of age, otherwise in robust health, and generally inclining to obesity. The direct attack may be preceded by left-sided pain low in the abdomen, coming in spells and associated with constipation. Sudden, more acute pain, general at first, later localized to the left iliac fossa, and more or less paroxysmal in type, marks the onset of definite symptoms. Vomiting is usually not marked unless the pain is very severe. There is more or less rigidity of the left rectus muscle. The previous constipation may now change to diarrhœa. Finally a mass is discovered developing to the left of the median line in the middle or lower quadrant of the abdomen. In women this mass is at times pelvic rather than abdominal.

In the *obstructive* cases the inflammatory symptoms are much less marked and the general symptoms of slowly progressive obstruction predominate. The condition may be readily confounded with carcinoma, especially as both conditions occur in advanced life; the formation of the tumor is, however, more rapid in the former. In diverticular obstruction there is usually a noticeable disharmony between the rather considerable size of the tumor and the lack of cachexia. Furthermore, the presence of blood in the stools would point strongly in favor of carcinoma.

The *treatment* of all forms of diverticula is purely surgical.

CONGENITAL FIXATION OF THE DUODENUM

Several varieties of congenital intraperitoneal bands or adhesions have been described. Those passing from the gall-bladder or the edges of its fossa to the duodenum, or across the duodenum to the transverse colon, may be of great clinical importance. Harris states that these bands are the abnormal folds of the left (ventral) layer of the caudal edge of the anterior mesogastrium. The duodenum may be compressed beneath such a band, or pulled upward by it to an abnormal position beneath the liver, so that progress of the duodenal contents is interfered with.

Niles[3] in a review of 39 cases found 31 males and 8 females, ranging in age from fifteen to sixty-seven years. All his patients had had digestive disturbances in infancy and childhood, and all had been constipated. Many patients with such fixation of the duodenum are of a neurasthenic type, and may complain of epigastric discomfort, flatulence, palpitation, tachycardia, headaches, and insomnia. Epigastric oppression one-half to two hours after meals is common; eructation, vomiting, and at times sharp epigastric or right hypochondriac pain may be noted. Often there

[1] *Trans. Amer. Surg. Assoc.*, 1907, p. 258.
[2] *Am. Jour. Med. Sc.*, 1904, **128**, 135.
[3] Trans. Assn. Am. Phys., 1924, **39**, 275.

is tenderness just to the right of the median line and midway between the costal margin and the umbilicus. There are no characteristic findings in the feces or gastric contents.

This condition is most often mistaken for chronic appendicitis, cholecystitis with adhesions, or peptic ulcer; when it occurs in neurasthenic individuals it is sometimes accompanied by a mucous colitis, and the symptoms are considered a manifestation of so-called intestinal intoxication. Roentgenologic examination is usually necessary for diagnosis, fluoroscopy being of special importance in this connection.

Actual duodenal obstruction is rare, but the patients if untreated often lapse into a state of semi-invalidism. Surgical treatment is usually successful (Homans recommends pyloroplasty in addition to division of the adhesions). Many patients can, however, be helped by the use of a bland diet, the food being finely divided, well cooked, and given in small amounts at frequent intervals. Rest with the hips elevated after meals, abdominal exercise and massage, and the wearing of a supportive belt are of value. Belladonna and bromides are recommended for accompanying spasm of the pylorus, duodenum, or sigmoid colon.

CARCINOMA OF THE INTESTINES

Compiling the statistics of Maydl, Nothnagel, Heimann, Zemann, and Müller, we find that of 26,340 cases of carcinoma in general, 2255, or 8.56 per cent., were in some portion of the intestines inclusive of the rectum. In determining the location of the tumor in the intestines there is a marked predominance of carcinoma of the colon and rectum. Combining the statistics of Maydl, Nothnagel, Zemann, Müller and Bryant, of the 659 instances of intestinal carcinoma, 6.22 per cent. were in the small intestines, 6.82 per cent. in the cecum and appendix, 22.76 per cent. in the colon, and 64.18 per cent. in the sigmoid and rectum. Carcinoma of the duodenum is frequent as compared with the ileum and jejunum, despite the great difference in the lengths. In the combined statistics of Maydl, Nothnagel, and Müller, of the 26 cases of carcinoma of the small intestine, 13 were in the duodenum and 13 in the ileum and jejunum. Rolleston collected 54 cases of primary cancer of the duodenum and but 19 of the jejunum and ileum. Russell, in 47 cases of carcinoma of the colon, found 23 in the cecum and ascending colon, 17 in the splenic flexure and sigmoid colon, and 7 in the transverse colon.

Carcinoma of the intestine is in the vast majority of cases primary. Secondary involvement may occur either by metastasis or by direct extension. Metastatic involvement is seldom noted, and when it does occur it is not infrequently as a part of a general carcinomatosis. Metastatic carcinoma of the intestines is usually multiple. The nodules have a tendency to locate in the mesentery just at its attachment to the intestines, thus producing multiple stenoses without involvement of the mucosa. Direct extension of cancer of a neighboring organ to the intestines is somewhat more common and occurs especially as a result of carcinoma of the pancreas, gall ducts, and pelvic viscera.

Sex is of little etiological significance. Males are apparently somewhat more frequently affected with carcinoma of the rectum and sigmoid, whereas this relative susceptibility is less evident in carcinoma of the upper portion of the tract. *Age* is probably a less important factor in carcinoma of the intestines than in carcinoma of almost any other portion of the body. The majority of cases occur in individuals over forty years of age, but not infrequently the condition is found in younger individuals. According to Maydl, one-sixth of all cases of carcinoma of the intestines occur between thirty and forty years of age, and one-seventh under thirty years of age. Bernoulli collected 37 cases in individuals under thirty years of age, and Nothnagel mentions 8 cases under twenty years of age. One was aged three and another three and a half years.

Pathology.—The majority of intestinal carcinomata are cylinder-celled adenocarcinomata taking their origin from the intestinal glands. Depending upon the relative proportions of the connective tissue to the epithelial elements, these tumors may be simple, medullary, or scirrhous. Of somewhat less frequent occurrence than cylinder-celled adenocarcinomata are cylinder-celled solid carcinomata and round-celled solid carcinomata, which may be simple, scirrhous, or medullary; colloid cancer may occur in the cylinder-celled or round-celled forms.

The macroscopic appearances are varied. Frequently the tumor assumes a saucer-like form having a necrotic ulcerated centre and elevated, indurated edges. Again, it is common to find the tumor extending about the entire lumen of the bowel in a girdle-like manner. Considerably rarer is the cauliflower-like mass of a papillary carcinoma. The tumors vary greatly in size. As the growth is dependent, to a great extent, upon the amount of epithelial tissue present, the larger forms are more commonly found among the medullary and simple carcinomata. The scirrhous forms seldom assume very great dimensions, and rarely undergo very extensive ulceration. They have a particular tendency to encircle the entire lumen of the bowel, and consequently stenosis is one of the most constant results Colloid cancers, relatively most common in the rectum, tend to infiltrate extensive areas.

Obstruction.– Both the degree and character of the obstruction differ materially in the various types of carcinoma and in individual cases. It may result in one of three ways. The carcinoma may produce an actual stricture of the bowel, most common in annular carcinoma, especially of the scirrhous form. The same result may occur in the case of an annular carcinoma of a softer variety when there is proliferation of the connective tissue of the bowel wall. In the second place, obstruction may result when the carcinoma so infiltrates the bowel wall as to materially increase the thickness of the intestinal wall and thus encroach upon the lumen. This is seen especially in colloid carcinoma, which tends to infiltrate the entire circumference. Lastly, obstruction may result when the carcinoma growing from the intestinal wall projects so far into the lumen as to occlude it.

Stagnation of the Intestinal Contents and Dilatation of the Intestine.—These are the direct result of the obstruction offered by the carcinoma. Not infrequently the stagnated contents just above the carcinoma

become inspissated and hard, so that in palpating this mass may be mistaken for the tumor itself. This error probably accounts for those cases in which a large tumor is diagnosed, but in which one of small size is found on operation or postmortem examination.

Dilatation of the intestine consequent upon carcinomatous obstruction may be either acute or chronic. Chronic dilatation results in those cases of slowly progressive obstruction in which the bowel above the point of obstruction has time to accommodate itself in part to the obstruction. Acute dilatation may result in those rare cases in which the obstruction is of rapid formation, but is much more commonly found as a terminal phenomenon in chronic dilatation. Hypertrophy of the wall cannot go on indefinitely, and a time occurs when the pressure of the peristalsis above and the obstruction below overcomes the resistance of the bowel wall and it balloons out. Occasionally in carcinoma of the colon acute dilatation of the cecum is found, although the portion of the colon above the obstruction is not dilated. The explanation probably lies in the fact that the cecum is subjected to the combined pressure of the peristalsis of the small intestines and the reverse peristalsis of the portion of the colon between the obstruction and the cecum. Rupture of the intestines in acute dilatation may occur.

Adhesions.—In the majority of cases of carcinoma of the intestine of some duration, adhesions are found between the peritoneal covering of the area involved and some other portion of the peritoneum. They may bind the intestines to the abdominal wall, or coils of intestines to each other or to any of the abdominal or pelvic viscera with which they come in contact. Frequently the adhesions are not limited to the region of the cancer but involve areas for some distance surrounding it, and at times the adhesive process produces a fusing or matting together of the entire abdominal and pelvic contents.

Perforation.—Perforation into the general peritoneal cavity may occur when the destructive processes are so rapid as to prevent the formation of adhesions. More common is perforation into a walled-off sac of the peritoneum or into one of the hollow abdominal or pelvic viscera. In this case there is always first a binding down of the carcinomatous intestine to the portion concerned, and subsequently a perforation. The rupture and the resulting fistula may be between two portions of the intestines, or between the intestine and the stomach, bladder, or uterus. Even perforation of the abdominal wall may occur.

Peritonitis.—A generalized peritonitis may result when perforation occurs into the general peritoneal cavity, or a localized peritoneal abscess forms when perforation occurs into a walled-off portion of the peritoneum. Peritonitis, either general or localized, may occur when there is no actual perforation, in all probability from increased permeability of the degenerated carcinomatous wall.

Metastasis.—The commonest seats of the metastases from intestinal carcinoma are the lymph nodes, liver, and peritoneum. There is some difference of opinion as to the frequency of metastasis, especially from the large intestine. Müller, Hausmann, Maydl, and Rupp claim that metastasis to the lymph glands occurs late in carcinoma of the large

intestines, and especially the rectum, while Hauser and others have found it early.

Symptoms.—Carcinoma of the Duodenum.—This is rather more frequent in males than in females. Of 54 cases, 41 were males. There was an average incidence of duodenal carcinoma of 0.033 per cent. in 151,201 collected autopsies (Deaver and Ravdin). It probably comprises between 2 and 3 per cent. of all primary intestinal carcinomas. Combined reports of Mayo, Rolleston, Geiser and Fenwick show 22.15 per cent. in the first part of the duodenum, 65.82 per cent. in the second, and 12.02 per cent. in the third.

Carcinoma of the duodenum can be classified into those of the first or superior horizontal portion, those of the second or descending portion, and those of the third or inferior horizontal portion. The symptoms usually differ materially with the position of the tumor. These differences are dependent primarily upon the seat of the tumor in its relation to the papilla of Vater, which is situated in the descending portion. On account of this relationship, Boas proposed the terms suprapapillary, circumpapillary, and infrapapillary carcinoma.

Suprapapillary carcinoma presents in a general way the symptoms of carcinoma of the pylorus, especially those due to the purely mechanical effects. There is dilatation of the stomach with vomiting of the stagnated contents. At times the vomitus contains blood. Since the gastric mucous membrane is not involved, free hydrochloric acid is usually present and lactic acid and other products of fermentation are not present. According to the Fenwicks, a tumor is palpable in 60 per cent. of the cases. When palpable it is less movable than carcinoma of the pylorus and is situated more to the right. Despite these points the diagnosis is frequently impossible.

Circumpapillary carcinoma, or carcinoma of the second portion of the duodenum, may present somewhat different symptoms depending upon whether the growth involves the papilla or not. If it does not the symptoms are either those of carcinoma above or below the papilla. When, however, as is usually the case, the papilla is involved, more characteristic symptoms present themselves. The symptoms of pyloric obstruction may be present, but in addition there is obstructive jaundice. The stools are clay-colored, the liver enlarged, usually tender, and digestive and other disturbances dependent upon the obstruction to the flow of the bile and pancreatic juice present themselves. These are not constant, for with ulceration the obstruction may be partially relieved and the escape of bile made possible. Subsequently the obstructive symptoms again present themselves, perhaps to be followed by another intermission. The ulceration gives access to an ascending infection of the biliary channels, so that a suppurative cholangeitis may supervene.

The severity of the gastric symptoms is dependent upon the degree of the stenosis caused by the cancer. If the growth should extend toward the pylorus, and at the same time ulceration in the neighborhood of the papilla occur, the symptoms of suprapapillary carcinoma would supervene. Similarly, if the growth extended toward the third portion of the duodenum, and ulceration about the papilla occurred, the symp-

toms of infrapapillary carcinoma would present themselves. In many of the cancers in this location, and especially in those in which obstructive jaundice is the predominant feature, the differentiation from carcinoma of the ampulla of Vater or of the lower end of the common duct or of the head of the pancreas is extremely difficult. The occurrence of intermissions in the jaundice and the development of a suppurative cholangeitis speak strongly for circumpapillary carcinoma. When a tumor is palpable it is felt as an immovable, hard mass deep in the right hypochondriac region near the midline. Either diarrhœa or constipation may be present and anemia and cachexia supervene.

Infrapapillary carcinoma characterizes itself by the symptoms of gastric obstruction associated with the vomiting of bile and pancreatic juice. The regurgitation of these fluids into the stomach neutralizes the acidity of its secretion, so that, although no free acid is found, the combined acidity may not be greatly decreased. The presence of the pancreatic secretion may be determined by its lypolitic action as well as its proteolytic action in alkaline media. The tumor is at times palpable as a firm, immovable mass near the midline.

Carcinoma of the Ileum and Jejunum.—Carcinoma of the ileum and jejunum presents symptoms for the most part similar to those of the first portion of the colon. There is constipation or alternating constipation and diarrhœa. More or less definite symptoms of obstruction may present themselves, but these are not so frequent or marked as in cancer of the colon, on account of the more fluid contents of the bowel in the small intestine. *Pain* is one of the most constant symptoms, and it is frequently of a colicky character. It is less definitely localized than is the pain of carcinoma of the large bowel. Occult blood is almost always present in the stools, and at times visible blood appears. Occasionally large hemorrhages occur. Although in some cases the tumor can be felt, this is by no means constant. When it can be felt it is characterized by its great movability unless it has been bound down by adhesions. On account of this, it is extremely prone to prolapse and is consequently not infrequently found in the lower abdomen or the pelvis. Cachexia and anemia sooner or later make their appearance. As a rule, these symptoms are more marked than in carcinoma of the large intestine, for, other things being equal, the nearer a carcinoma is to the stomach the more profound are the cachexia and anemia.

Carcinoma of the Colon.—Pain is a frequent but not invariable symptom. Some cases run almost the entire course, even to the development of a palpable tumor and marked cachexia, without the occurrence of pain. The majority of cases, however, manifest some degree of pain. It may vary from a vague sense of discomfort to a symptom of great severity, but seldom reaches the extreme until obstruction becomes marked or absolute. Early in the course the patient occasionally complains of diffuse abdominal pain without definite localization. Frequently accompanying this is a sense of pressure or dragging in the abdomen. Later the pain becomes more localized. Occasionally the pain is referred to distant parts, so that a patient with carcinoma of the cecum may complain of pain in the left iliac fossa, or *vice versa*. This should con-

stantly be borne in mind to avoid errors in localization in case of operation. Another confusing phenomenon is referred pain along the course of the anterior crural or sciatic nerves due to pressure on the intra-abdominal plexuses.

The variety of pain that is of greatest significance in the diagnosis of carcinoma of the intestine is *colic*, due to the progressive stenosis and the consequent distention and tonic peristaltic activity of the intestines above the stenosis. Not infrequently these paroxysms constitute the first symptom. Generally the pain is diffuse throughout the abdomen, although occasionally the patient describes it as more or less localized. At times a cathartic brings on the first paroxysm of colic. The pain may shift from one position to another until it comes to an abrupt termination with a violent cramp, indicating the location of the growth.

A feature that practically always accompanies these attacks of colic is *constipation*. It is one of the most constant and frequently one of the earliest symptoms of intestinal carcinoma, and its occurrence in an individual past middle life should always excite one's suspicion. It is progressive but is occasionally interrupted by periods of normal activity of the bowels. These interruptions are sometimes due to ulceration of the tumor reëstablishing the lumen previously stenosed, and such periods may be accompanied by the appearance of blood, mucus, and pus in the stools. Relief of constipation may be due also to a more fluid condition of the intestinal contents. Again, periods of diarrhœa are by no means infrequent in intestinal cancer.

Tumor.—A palpable tumor is the most reliable and most important sign but its detection is not essential to the diagnosis. Some cases run their entire course without the development of a palpable tumor. In the majority of cases careful and repeated examinations reveal a mass. The tumor may vary in size from that of a large nut to that of a child's head. In consistency it contrasts markedly with the surrounding abdominal contents, frequently feeling as firm as cartilage. It is round or irregular and its surface may be smooth or nodular. The infiltrating tumors, when they involve extensive areas of the bowel, give the impression of a thick, solid cord. When a tumor is very small, percussion over it elicits a note not differing from that of the surrounding intestines. The larger tumors are usually dull to percussion. Pressure usually causes more or less tenderness, proportionate to the degree of spontaneous pain. The movability of carcinoma of the large intestine, unless it be bound down by adhesions, is a most characteristic feature. This is especially true of carcinoma of the transverse colon and the sigmoid, but almost equally so of carcinoma of other portions of the large bowel.

A condition intimately associated with the tumor of intestinal carcinoma, and prone to cause confusion with it, is the tendency to fecal impaction above the point of obstruction. It is not unusual for this mass to become so inspissated and compact as to cause the greatest difficulty in differentiating it from the carcinoma and lead to great misconceptions of the size of the growth. Usually, however, the consistency of this fecal mass is more doughy than that of the carcinoma, and unless the stenosis be complete, laxatives and enemata may clear

up the question. Other phenomena that can at times be clearly observed are active peristalsis and distention of the portions of the bowel just above the carcinoma. They are both dependent upon the degree of the stenosis. In patients with thin abdominal walls, in whom hypertrophy of the intestines has occurred above the stenosed area, active peristaltic waves are frequently visible and at times serve as a means of localizing the growth. In carcinoma of the cecum the peristalsis of the small intestine is seen in the central and lower portions of the abdomen, while in carcinoma of the lower portion of the colon these movements are seen in the course of the large bowel.

Gaseous distention is at times so general that the portion involved cannot be determined. In other cases, however, this distention is limited to the segment immediately above the carcinoma, and its observation is then of considerable value as to the seat of the growth. If the distention is found to extend as far as the sigmoid, this would point to the latter portion being the seat of the involvement, whereas if only the transverse and ascending portions of the colon are distended, the localization would in all probability be at the splenic flexure. In carcinoma of the hepatic flexure the ascending colon would be the natural seat of the distention.

The feces occasionally furnish valuable information of the possible existence of a carcinoma of the large bowel. The form of the feces is dependent upon the degree of the stenosis affected by the carcinoma. When the carcinoma is low down and the stenosis is of high degree, the feces are generally of small diameter and either circular or ribbon-shaped, or rudely rectangular in cross-section. Blood, pus, and mucus are not of themselves diagnostic of carcinoma but indicative of an ulcerative process in the intestines. Blood may be present even when ulceration has not occurred. In such cases it proceeds from small erosions of the mucous membrane, sometimes the result of the mechanical irritation of the fecal masses. Pus is always an indication that ulceration has occurred. The association of pus and blood is of considerable diagnostic significance, for they occur together only in the most severe forms of intestinal ulceration. Shreds of tissue with the histological features of carcinoma may be present, and are of the greatest diagnostic significance. They are, of course, present only when ulceration has occurred.

Cachexia and anemia are constant features of the later stages, but are usually of later development in carcinoma of the large intestine than in carcinoma of the small intestine or stomach.

Roentgenology furnishes a very important aid in diagnosis.

Complications.—Acute intestinal obstruction may occur at any time from kinking by bands in the neighborhood of the carcinoma, or volvulus or intussusception induced by the growth, or from the impaction of a foreign body in the partially stenosed lumen, or the simple paralysis of the bowel above the stenosis. Peritonitis may result from rupture or from direct extension through the ulcerated intestinal wall. A localized peritoneal abscess may occur when adhesions have formed around the site of the peritonitis. Perforation of a carcinoma of the large intestine into another hollow abdominal viscus occasionally occurs. Perforation of a carcinoma of the transverse colon into the stomach forming a gastro-

colic fistula can be recognized by the presence of fecal vomiting and diarrhœa in which the stools contain undigested food particles. Perforation into another portion of the intestine may occur, and it is a peculiar fact that perforation of a carcinoma of the large intestine is more prone to occur into another portion of the large intestine than into the small intestine. Perforation into the bladder can usually be recognized by the discharge of fecal elements with the urine.

Treatment.—When feasible, surgical treatment is employed, whether it be for removal of the growth or to overcome the results of stenosis. When surgical intervention cannot be resorted to, much can be done for the relief of the patient. The principal object is the prevention of fecal accumulation above the tumor. Of the means to guard against it the most important is the administration of such foods as contain a minimum of waste material, and in such form as to be most easily digested and absorbed. Small doses of laxatives may be frequently administered, and their action may be furthered by oil enemata. Roentgen-ray therapy may be tried in inoperable cases.

SARCOMA AND LYMPHOSARCOMA OF THE INTESTINES

Sarcomatous and lymphosarcomatous involvement of the intestines are much rarer than carcinomatous. Whereas, among the autopsies in the General Hospital of Vienna, from the years 1882 to 1893, 243 carcinomata of the intestines were found, there were but 3 cases of sarcoma of the intestines and 9 cases of lymphosarcoma. In Bern 41 cases of carcinoma of the intestines were found to 1 of sarcoma. Sarcoma and lymphosarcoma involve the small intestine at least equally as frequently as they do the large intestine. Of 32 cases of intestinal sarcoma selected by Krueger, 16 were of the small intestine and 16 of the large intestine. In the 12 cases of sarcoma and lymphosarcoma occurring in Vienna, 8 involved the small intestine and 4 the large intestine.

The various portions of the small intestine are apparently involved with about equal frequency. In a series of cases collected by Libman, 15 were in the duodenum, 18 in the jejunum, and 14 in the ileum. In the large intestine the rectum is most frequently involved, and next in frequency the ileocecal region. Jopson and White collected 22 cases of sarcoma and lymphosarcoma involving the large intestine.

Lymphosarcoma apparently takes its origin from the lymphatic tissue of the intestinal wall and has a great tendency to involve extensive areas of the wall by a process of infiltration. Sarcomata arise from the connective tissue of the submucous layer of the intestinal wall. Histologically, the most frequent form is the small round-celled sarcoma, but large round-celled, spindle-celled, and mixed forms may occur. These tumors also have a marked tendency to infiltrate extensive areas of the bowel wall, but at times they are more globular in form, when they may attain the size of a child's head. When they attain the latter proportions they frequently undergo central softening. They may occur at any age but are most frequent under forty years of age. They are commoner in males than in females.

Symptoms.—The symptoms of sarcoma of the intestines differ materially from those of carcinoma. In sarcoma the local symptoms remain in the background, and usually attract attention long after the constitutional effect is noticed because there is not the tendency to stenosis of the bowel in sarcoma and lymphosarcoma as in carcinoma. Sarcoma and lymphosarcoma invade the intestinal wall and tend to extend longitudinally along the bowel or into the muscular coat, causing weakening and consequent dilatation, but there is little tendency to intestinal stenosis. In the majority of cases there is marked wasting and anemia before the symptoms point to any extent to the intestines. In a minority of cases the symptoms of obstruction may occur as a result of the growth of the tumor toward the intestinal lumen, or the destruction of the muscular elements of the wall may lead to paresis and consequent obstruction. Pain and diarrhœa are occasional symptoms Blood, either occult or visible, may be found in the feces. Occasionally fever as high as 101° and 102° F., is an accompaniment of sarcoma or lymphosarcoma of the intestines. Local examination will, in the majority of cases, reveal a tumor. Generally, this is in the nature of greatly thickened coils of intestines, but occasionally it is of a more circumscribed nature. Metastasis to the mesenteric lymphatic nodes may occasion greatly increased tumor masses. The duration contrasts with that of carcinoma of the intestines; in the majority of cases the patient dies in from four to eight months after the onset of symptoms.

Treatment.—Excision of the growth offers the only possibility of cure. Medical treatment can be directed only to the alleviation of symptoms.

BENIGN TUMORS OF THE INTESTINES

Benign tumors of the intestines are of rare occurrence. In many cases they present no symptoms whatever, the first indication of their presence being their observation at autopsy. In other cases they give rise to various symptoms, but these are seldom characteristic.

Adenoma.—These are the most frequent benign neoplasms of the intestines. The tumors take their origin from the glands of Brunner and Lieberkühn, and are usually either polypoid or papillomatous, more frequently the former. Their size varies from that of a pea to that of an orange; they are firm or soft but usually vascular, and bleed on handling. They are usually multiple. Luschka has reported a case in which he counted over a thousand tumors. This condition of multiple intestinal adenomas is termed by Hauser "polyposis intestinalis adenomatosa." The tumors may be diffusely distributed, but are usually most numerous in the colon and rectum. In children they tend to prolapse, and thus may become gangrenous or give rise to serious hemorrhages. Simple polypi are thought to be the result of mucosal hypertrophy between areas of fibrous scar tissue following ulceration. Not infrequently polypoid adenomas give rise to carcinomas; Quénu and Landal found carcinoma in 20 of 42 cases and of 61 cases collected by Doering and by Soper, 43 per cent. showed carcinoma. Multiple polypoid adenomas are most frequent in children from four to seven years of age.

In 4 of 13 cases reported by Post the condition appeared to be hereditary, and Niewack reported cases showing a family predisposition.

Adenomas of Endometrial Type.—Sampson has described the implantation of adenomas on the serous surfaces of the intestines (rectum, sigmoid, small intestine and appendix) following the rupture of ovarian hematomas containing endometrial cells. This endometrial tissue is thought to reach the ovary through the Fallopian tubes, or possibly to represent misplaced Müllerian epithelium. He found intestinal implantation in over 50 per cent of such instances of aberrant endometrium. The tumors may resemble carcinoma on gross inspection. They sometimes penetrate to the lumen of the bowel and give rise to symptoms, which may be more marked during the menses due to filling of the tumors with blood. They usually occur between the age of thirty and the menopause and are thought by Sampson to disappear after removal of the uterus, tubes and ovaries, or after the menopause.

Lipoma.—These may be broad-based or pedunculated, and submucous or subserous; they may be small or as large as a child's head. When of the latter proportions they frequently produce obstruction; somewhat smaller growths may induce intussusception. They are more frequent in the large than in the small intestine. Of 36 cases collected by Dewis, 19 were in the large intestine. The subserous lipoma frequently develops from the epiploic appendages. When pedunculated, the pedicle may atrophy and the growth may lie free in the peritoneal cavity. A submucous lipoma may become detached and be expelled by the rectum.

Myoma.—Myoma of the intestines is rare. It occurs oftener in the small than in the large intestine and may be internal or external. The former probably takes its origin from the muscularis mucosa, the latter from the external muscular coat of the intestines. Steiner, in his exhaustive analysis of benign tumors of the intestines, reported 19 cases of internal and 15 of external myoma. They are more commonly found in the ileum and jejunum than in the duodenum and large intestine. These tumors may have a broad, flat base and appear more as localized thickenings of the intestinal wall, or they may be pedunculated, thus taking the form of a polyp. Occasionally there is an extensive distribution of fibrous tissue with the muscular tissue (fibromyoma).

Hemangioma and Lymphangioma.—Hemangioma and lymphangioma are rare. McCallum collected 6 cases of hemangioma of the small intestine. They are usually cavernous as distinguished from telangiectatic hemangiomas; as a rule, they are small, flat, and multiple.

Neurofibromas, fibromyxomas and teratomas have been reported.

Symptoms.—Benign tumors of the intestines may not give any indication of their presence or they may present symptoms of a more or less definite character, and at times give rise to conditions of great severity. In multiple intestinal polyposis, hemorrhage and diarrhœa are the most frequent symptoms. If the lesions are located in the colon and rectum, tenesmus may be associated. The stools frequently contain large quantities of mucus. A rectal examination should never be neglected, as not infrequently the diagnosis will be made by finding numbers of the polyps springing from the wall of the rectum. In these cases the

polyps are especially liable to constant irritation, and the presence of blood is a frequent symptom. When these adenomatous polyps undergo carcinomatous degeneration the symptoms of cachexia appear.

In myoma, fibroma, and lipoma, hemorrhage and frequent stools, with mucus, may be the predominant symptoms, but they occur much less frequently than in the multiple polypoid tumors. If the tumor is small and situated above the rectum or sigmoid, it usually remains undiscovered. If it is of larger size it may produce a slowly progressive obstruction, or, by inducing intussusception, cause acute obstruction. Steiner records 7 instances of intussusception in 18 cases of large intestinal myoma. When the tumor is of considerable size it can frequently be palpated as a firm, nodular, rather freely movable mass. If it is in the lower part of the large intestine and extends downward it may be palpated or seen in the rectum. Angioma may give rise to extensive hemorrhages. It is impossible to make more than a presumptive diagnosis on the basis of intestinal hemorrhages in an individual previously healthy and in whom no other cause can be determined.

Treatment.—The internal treatment of benign tumors of the intestines is limited to the treatment of the various symptoms. When, however, the symptoms are of sufficient severity or when the tumors are situated in the rectum, surgical treatment is warranted. In case the tumor causes obstruction, operation must be undertaken. In case of hemorrhage of alarming severity from angioma or other benign tumor, operation may be employed. In those instances in which benign tumors are found in the rectum, even when they give rise to no symptoms, they should be removed on account of their tendency to undergo malignant change, as well as the possibility of dangerous hemorrhage.

MESENTERIC EMBOLISM AND THROMBOSIS

In an analysis of 214 cases (Jackson, Porter, and Quimby, 1907) there were 197 instances in which an accurate study of the anatomical details was obtainable. Among these, 120, or 61 per cent., were cases of arterial obstruction, and 77, or 39 per cent., of venous obstruction. Embolism is considerably more frequent than thrombosis, the former condition having been present in 63 of 83 cases studied by Gallavardin.

Etiology.—Endocarditis and atheromatous conditions of the aorta or of the trunks of the mesenteric arteries are the important conditions antedating embolism. *Arterial thrombosis* is liable to occur when there has been severe enteritis or infective conditions of the intestinal tract, as a result of which bacterial invasion into the bloodvessels takes place. Litten claimed that he had found thrombotic occlusion of the arteries as a consequence of diseased conditions of the arterial lining, but the correctness of his observation has been doubted. Syphilitic endarteritis has also been claimed as a cause of thrombosis, as has direct abdominal injury. *Venous thrombosis* may occur as the result of cirrhosis of the liver, thrombosis of the portal vein, and other conditions causing stasis in the portal circulation.

Embolism and thrombosis of the mesenteric vessels occur much more

frequently in men than in women. Jackson, Porter, and Quimby found 64 per cent. in men and 36 per cent. in women. Over half their cases were observed between the ages of thirty and sixty years.

Pathology.—The superior mesenteric artery is affected much more frequently than the inferior. The occlusion may involve the trunk of the vessel or one of the terminal branches. Sometimes it affects only the small terminals within the intestinal wall itself. In the last-named cases small ulcerations of the mucosa are met with. The results of venous thrombosis are practically indistinguishable from those of arterial occlusion. There may be a single occlusion of the trunk vessel, or multiple obstructions of small branches. In either case changes occur in the mesentery and bowel embraced in the distribution of the obstructed vessel. The mesentery and the bowel become intensely engorged with blood and assume a dark red and soon almost black color. Hemorrhagic extravasations take place into the tissues, and exudations of hemorrhagic fluid into the abdominal cavity and into the lumen of the bowel occur. The whole lesion is practically a hemorrhagic infarction of the affected area. The affected tissues may undergo rapid necrosis or gangrene, and perforative peritonitis may ensue. In the majority of cases a line of demarcation is observed.

The lesions are usually met with in the small intestine, which is supplied by the superior mesenteric artery. In the rare cases in which the inferior mesenteric vessel is involved the lesions are situated in the large bowel. Partial restoration, through the development of a collateral circulation, has been observed in a few instances.

Symptoms.—Two groups of cases are distinguishable, an acute and a chronic, the majority of the cases belonging to the former. In these there is sudden abdominal cramp or colicky pain, followed by nausea and vomiting. The vomitus at first consists of the contents of the stomach, but very speedily becomes hemorrhagic. Very soon diarrhœa sets in and also becomes of hemorrhagic character. In other cases hemorrhage does not occur, and the symptoms are practically those of an acute intestinal obstruction caused by the paralytic condition of the affected portion of the bowel. The patient's temperature usually falls decidedly, he breaks into profuse perspiration, and frequently sinks into more or less profound collapse.

In some cases pain is wanting, and the earliest symptom may be a hemorrhagic diarrhœa, but pain is usually conspicious. In some instances the patient may suffer with repeated attacks of colicky pain, over a considerable period of time, without characteristic symptoms of vascular occlusion. In the more acute cases, intense abdominal pain of almost continuous character, or recurring in paroxysms, is met with. In over one-half the cases the pain is general. In the others it is limited to one or another region of the abdomen. Local tenderness on pressure may develop and sometimes becomes extreme when peritonitis has set in.

Hemorrhagic diarrhœa is the most conspicuous and significant sign, although not always present. The amount of blood sometimes becomes excessive; and usually there is rapid succession of movements each containing a considerable quantity of blood. When the hemorrhage is

marked, the blood may be quickly passed and is only slightly altered. In other cases, black, tarry movements indicate a longer retention within the bowel. Distention of the affected area of the bowel sometimes develops rapidly, and general abdominal distention occurs in the cases in which intestinal obstruction is the important consequence of the vascular occlusion. In some instances a palpable tumor has been discovered, the mass being caused by the infiltrated mesentery and bowel.

In the more chronic cases, which include most of the instances of venous thrombosis, as well as some cases of arterial occlusion, the onset may be insidious and the symptoms of a remittent type. At times there are no abdominal symptoms or, at most, they are vague and indefinite.

The clinical course may be exceedingly rapid. Jackson, Porter, and Quimby found that 20 per cent. of the cases of either arterial or venous occlusion had a duration of but twenty-four hours; and 18 per cent. and 22 per cent. of the venous and arterial cases, respectively, a duration of but two days. In 8 and 10 per cent., respectively, the duration was three days. Of the prolonged cases, those due to venous closure showed gradual and continuous progression, while the arterial cases were more apt to present interrupted attacks. In the very acute cases, after the initial pain and vomiting, rapid distention of the abdomen, cessation of peristalsis, and speedy death mark the course.

Diagnosis.—The rules laid down by Gerhardt are still followed with advantage: (1) There must be a source of embolism. (2) Copious intestinal hemorrhage unexplained by organic disease of the bowel or by portal obstruction. (3) A rapid and marked fall of the temperature. (4) More or less severe colicky abdominal pains. (5) Distention of the abdomen and the accumulation of free abdominal fluid. (6) The occurrence of embolism elsewhere, before or simultaneous with obstruction of the mesenteric vessels. (7) The discovery of a palpable mass.

Prognosis.—With few exceptions, the disease terminates fatally. In the statistics before quoted there are recorded 14 cases in which the diagnosis seemed reasonably accurate and in which recovery ensued. This favorable termination can occur only when a collateral circulation is speedily established.

Treatment.—This is purely surgical. Jackson, Porter, and Quimby refer to 47 cases in which an exploratory laparotomy was undertaken. The mortality in these cases was 92 per cent. Four patients recovered.

ARTERIOSCLEROTIC INTESTINAL DISTURBANCES

Certain painful conditions of the intestine are occasionally met with in the aged and arteriosclerotic, and are of some importance on account of their simulation of organic or inflammatory disease of the bowel. The onset may be abrupt, like that of acute intestinal disturbance, and pain may be severe. Usually there is constipation; and sometimes this is obstinate. Later, and especially after the use of laxatives, diarrhœa may set in. Localized soreness or tenderness may be discovered, but there is rarely marked rigidity of the muscles. The nature of these conditions is uncertain. In some cases, doubtless, obstructive conditions

of the circulation play an important part. In a case under the observation of the writer, after a number of attacks, death occurred from a severe paroxysm with obstinate constipation, which was followed by the development of uremia. At autopsy a partial obstruction of a branch of the superior mesenteric artery was found; and the section of bowel supplied by this was intensely engorged with blood. There was not complete obstruction, and no actual hemorrhagic infarction. Ortner has referred to cases somewhat resembling this, under the title of Intermittent Angiosclerotic Dyspragia of the Intestines. He suggests the resemblance to intermittent claudication, and refers particularly to the intermittent character of the symptoms.

MUCOUS COLITIS

Definition. The term mucous colitis is applied to a condition in which the patient suffers with various symptoms of disturbance of the stomach and bowels and with the regular or periodic discharge of masses of mucus or mucomembranous shreds or casts of the bowel. The terms *membranous colitis*, *tubular diarrhœa*, *mucous colic*, and *mucous diarrhœa* have been applied, and sometimes, although with insufficient justification, a distinction has been drawn between these as being different forms of disease. It is possible to distinguish cases in which mucous or membranous diarrhœa occur as an independent affection and those in which it is secondary to some other disease of the bowel, but there is no fundamental difference between the cases in which a discharge of masses of gelatinous mucus occurs and those in which membranes or casts of the bowel are met with.

Etiology.—The disease is most common in the middle period of life—that is, between thirty and fifty years; but it sometimes occurs in children or those below thirty years, and occasionally persists after fifty years. It is more common in women than in men, the proportion probably being 5 or 10 to 1. The disease affects persons of a better station of life more frequently than the poor, and is commonly associated with a nervous temperament or with distinct nervous disease. Not rarely it develops in hysterical or neurasthenic women, particularly if they have suffered with dyspeptic symptoms and constipation. It may follow after other forms of intestinal disease, the secondary variety being a frequent accompaniment of such diseases as enteroptosis, chronic appendicitis, partial intestinal obstruction, dysentery, tumors, and long-standing constipation.

The direct cause probably varies greatly. Nutritional conditions, such as are met with in those of reduced strength and those having nervous diseases, seem to play a predisposing role. Some authors regard the condition simply as an intestinal neurosis with excessive mucus formation (*myxoneurosis*). Others have the contrary view that the nervous manifestations are entirely secondary and that the disease is essentially an inflammatory condition with excessive tendency to mucus formation. It has been claimed that certain bacteria play a part, among other organisms being the *Bacillus coli*.

Pathology.—The characteristic feature is the formation of excessive quantities of mucus. This may occur as masses or balls of gelatinous character, which may be discharged as such or mixed with the fecal matter; or, more characteristically, the mucus may attach itself to the wall of the bowel and subsequently be discharged as skins, shreds, tape-like bands, or casts representing a mould of the bowel. Probably the commonest form is that in which the skins or shreds of membrane are discharged in masses or mixed with fecal matter. The shreds or casts are somewhat laminated, and may show depressions corresponding with the openings of the glands of the mucous membrane. Epithelial cells may be found on the outer surface. The mucous membrane itself may present an inflamed appearance, but usually there is surprisingly little evidence of any structural disease. Often an atonic dilatation of the colon is observed, but in other cases a firm tonic contraction of the bowel causes a narrowing of the lumen and an apparent thickening of the wall.

Symptoms.—These are gastric, intestinal, nervous, and nutritional. Usually the patient complains of some form of indigestion or dyspepsia. The appetite is poor and capricious; and the patient accustoms herself to greater and greater restriction of diet, as the result of attempting to find a dietary that will not cause discomfort. Distention of the stomach, flatulence, heaviness, or pain after eating, nausea, and other gastric symptoms may occur. Sometimes pronounced manifestations of various forms of nervous dyspepsia are present.

Among the intestinal symptoms, constipation and the discharge of characteristic mucus- or membrane-containing stools are most important. The majority of patients are constipated, and the discharge of mucus or membrane occurs from time to time, attended with painful paroxysms of varying grades of severity. When large casts or abundant membranous shreds are passed, an attack of abdominal pain of great violence may precede, suggesting some form of intensely acute inflammatory trouble. After the passage of the mucus or membrane the painful attack ceases, but a rawness or soreness may persist for some time. In the majority of cases such painful paroxysms are exceptional, and not rarely the passage of the mucus or membrane is accompanied by a relief of previous symptoms, such as intestinal distention, abdominal discomfort, depression, etc. Occasionally, instead of constipation, the patient suffers with continued looseness of the bowels and the passage of large quantities of mucus mixed with fecal matter. Sometimes when shreds of membrane or casts are passed there may be a certain amount of blood streaking the membranes; and in exceptional instances a considerable quantity of blood may be discharged.

On examination, the abdomen is distended or scaphoid. Preceding attacks, there may be increasing distention of the colon, which later gives place to a contracted or scaphoid condition; but in many instances distention is wanting at all times, and on direct examination the colon is found contracted as a hard tube. It may be possible to palpate the ascending and descending colon and the sigmoid flexure. The transverse colon is less commonly palpable.

The patient may for a long time suffer with gastric and vague intestinal

symptoms and constipation, and may become increasingly nervous, before the characteristic symptoms of mucus- or membrane-formation develop. In such cases the mucous colitis is probably secondary.

The *nervous* manifestations are usually striking. It is difficult to determine to what degree these are the result or the cause of the condition. Nearly all patients with this condition are depressed, gloomy, irritable, and of low vitality. Distinct hypochondriacal tendencies may be marked, and sometimes the patient becomes actually melancholy. Reflex nervous disturbances may occur, such as weakness and irregularity of the heart action, neuralgias, headaches, migraine, etc.

The *nutritional* condition corresponds with the state of the gastro-intestinal tract and of the nervous system. Most of the patients are thin or emaciated, and many become progressively more so with its persistence. Sometimes, however, typical and progressive mucous colitis may occur in neurasthenic or hysterical subjects, who show no loss of weight at all commensurate with the disturbance. The patient presents an appearance of anemia which, however, is frequently deceptive, since the blood may be practically normal.

Complications.—In some cases the passage of *intestinal sand* is observed. This presents itself as a reddish deposit, resembling brick-dust, or as a grayish or white powder, which consists of phosphate and oxalate and carbonate of calcium with magnesium and iron. A small amount may be passed with each movement, or sometimes large quantities may be discharged from time to time.

In some cases intense soreness of the bowels and probably actual ulceration result from the separation of firm, membranous formations. In these cases the passage of the membrane may be preceded by painful paroxysms of great violence, and may be attended with the discharge of small or large quantities of blood. After the attack, local soreness in the left side or general abdominal tenderness may persist.

Various disorders of the pelvic organs occur in women suffering with this disease; among others, endometritis, menstrual irregularities, dysmenorrhœa, and neuralgic affections localized in the pelvic region. Occasionally, membranous dysmenorrhœa and membranous cystitis have been found combined with membranous colitis.

Diagnosis.—Examination of the stools alone enables the physician to diagnose the condition. Neglect of such examination may be the cause of regarding cases of mucous colitis as various sorts of primary nervous disease. Secondary mucous or membranous colitis associated with organic diseases of the bowel, such as chronic appendicitis, adhesions, diverticula, and tumors or strictures, may be indistinguishable from the primary variety. Usually, however, the organic conditions named serve to localize the symptoms and indicate the association.

Prognosis.—Mucous colitis is essentially a chronic disease, which tends to continue and increase, although it is not often directly fatal. The general health may be so greatly undermined and nervous vitality so impaired that the patient falls a prey to other conditions. A large proportion of cases (perhaps 50 per cent.) eventually improve to such an extent that, although the health of the individual may be permanently

impaired, the actual disease no longer manifests itself. In other cases the disease persists with more or less unabated intensity up to the time of death. Under continuous treatment some improvement is usually obtained, but the chronicity of the affection is such that few patients continue the treatment long enough to obtain the full result possible.

Treatment.—The general hygiene and the diet are the most important considerations. Outdoor exercise and suitable occupation are essential. The majority of patients suffer from a sedentary life and a lack of suitable occupation. Not rarely, forced exercise may bring about decided relief, particularly in those cases in which general nervous depression has been augmented by lack of occupation. In some cases, active treatment of the gastric digestion may prove helpful. Increasing doses of nux vomica with bicarbonate of soda or the use of digestives may be beneficial.

The dietary treatment may follow one of several rather different plans. Certain authors insist upon the necessity of limiting the dietary decidedly so as to exclude all irritating and unabsorbable matters. They, therefore, exclude vegetables containing large amounts of cellulose and prescribe mainly farinaceous articles with milk, eggs, and a limited amount of meat—all of which should be so prepared as to be rather semi-solid or liquid. They advise in addition a rather careful study of the tolerance of each patient for the different articles of diet allowed. On the contrary, other authors following von Noorden advise a rather coarse dietary containing rye bread, whole wheat bread, vegetables rich in cellulose, raw fruit, etc. The immediate effect of the former plan is undoubtedly more satisfactory in most cases and is better, though in some cases the coarser diet may be eventually the best. Whatever plan is adopted it is advisable to see that the patient has sufficient nourishment.

It is important that the intestinal drainage should be maintained, and when constipation is marked some form of laxative is helpful. In many cases the occasional administration of castor oil relieves the patient for some time, and may have a lasting beneficial effect. In some, the administration of very small doses of castor oil several times daily, in combination with salol, beta-naphtol, guaiacol carbonate, or calomel in fractional doses, may be beneficial. Now and then it is advisable to administer a saline purgative or to use medicinal waters for the same purpose. Paraffin oil in doses of 1 to 2 teaspoonfuls three times daily, or of 1 or 2 tablespoonfuls at night, often gives excellent results if continued for considerable periods.

Colonic douches with simple saline solution, or with water containing fluidextract of hamamelis, small amounts of quinine or nitrate of silver (1 to 5000), may have a beneficial effect. It is rarely desirable, however, to persist in direct colonic medication or flushing, as too long a continuance of this plan of treatment may cause a return of the symptoms, and even an aggravation of them. Some patients are helped by the gentle injection into the colon of 10 or 12 ounces of olive or cottonseed oil at bedtime, to be retained during the night.

Local treatment of the abdomen is useful in some cases. Abdominal massage given by a skilful manipulator, external or intra-intestinal

electricity, and high-frequency currents have sometimes been used with advantage. Wright and others have treated patients by vaccination with killed cultures of the *Bacillus coli*. This method, however, rests upon no certain foundation.

Surgical measures have been used with advantage. Occasionally the removal of a chronically inflamed and adherent appendix has been followed by remarkable improvement. Some obstinate cases have been treated by attaching the tip of the appendix to an abdominal opening and flushing out the bowel daily, or at stated intervals. In other cases an artificial anus has been made in the right iliac region, and has been used to flush the colon thoroughly. The seriousness of such an operation and its generally objectionable features militate against its frequent employment. It has also been suggested that the ileum be anastomosed with the rectum.

CHAPTER XI

SPRUE

By EDWARD JENNER WOOD, M.D.

Sprue is a chronic disease process characterized by a distinctive sore tongue and mouth, a peculiar type of diarrhœa with stools suggestive of pancreatic insufficiency in the bulkiness and high fat content, a marked anemia which is suggestive of a primary process and loss of flesh. It is further characterized by a tendency to remissions and exacerbations, its greater prevalence in tropical and subtropical sections, its occurrence in newcomers into these sections from the temperate zone, and its greater incidence among the higher classes of the population than among the poor.

Sprue is said to be endemic in South China and the East Indies, in India and Ceylon, in the West Indies chiefly in Porto Rico, in east and south Australia, in Japan, in Korea and in the Philippine Islands. Certain tropical regions, as West Africa, have never been invaded by it. Its reported incidence is often a matter of its recognition. Hitherto sprue has not been thought to occur in the United States although, since interest has been aroused in it, there is no longer any doubt that it is of frequent occurrence.

It was formerly supposed that sprue never occurred among natives in the tropics but always in newcomers from colder climates but Manson-Bahr and other observers have shown conclusively that it does attack natives. Certainly it occurs frequently in the southern states among individuals who have never been out of their home states. Its occurrence in the negro race must be exceedingly rare. In a large series of cases observed in North Carolina the writer has never observed such an instance.

The position of sprue is still unsettled, its very nature being still largely a matter of speculation. Manson regarded it as a distinct disease entity while others look on it as a secondary process following such intestinal disturbances as amœbic or chronic bacillary dysentery. Many conditions seem to have been confused with it. Chief among these is Cochin-China diarrhœa which is an infestation with *Strongyloides stercoralis*. A possible relationship of sprue to Addisonian anemia has been suggested. L. W. Smith in the Philippines found blood changes in sprue which are usually associated with so-called aplastic anemia. The writer has suggested the possibility that sprue and Addisonian anemia may be types of a single condition. There are cases of sprue which cannot be differentiated from Addisonian anemia on clinical grounds. The blood picture in sprue often adds to the difficulty. It is stated that cases classified as sprue have later presented an undoubted picture of Addisonian anemia. Recently the writer observed subacute combined degeneration of the spinal cord in sprue, which hitherto has been one of the points of distinction between

the two conditions. Sir Byrom Bramwell has found in sprue and in Addisonian anemia several points of close similarity in the pathological changes which he regarded as suggesting the results of similar harmful agencies.

Etiology.—Residence in the tropics by new-comers from colder sections has been regarded in the past as practically essential for the production of sprue. Englishmen in the eastern tropics and Americans in the Philippines made up a large part of the list of victims. American missionaries in certain sections of China, in Korea and in numerous other points in the tropical East and in certain portions of the West Indies have suffered seriously. Recent study has demonstrated that the disease does occur among natives and this is particularly well demonstrated in the southern states, but it must be admitted that the new-comer is the chief victim. The disease occurs as often, if not more so, in subtropical as in tropical sections but the first indication of the disease may not be noted until years after the return from a tropical or subtropical sojourn. In 1 case the patient, who was a resident of Boston for many years, had lived in North Carolina twenty-five years before the occurrence of sprue. Usually the patient has resided in the warm climate for a number of years but occasionally the disease develops after a very brief sojourn.

Manson emphasized the part played by many exhausting diseases especially of the intestinal tract. Among the predisposing factors have been included child-bearing, miscarriages and other gynecological conditions especially those attended with profuse hemorrhage. Prolonged lactation, syphilis and its treatment by mercury and iodides have been regarded as provocative factors. It is probable that the parasitic intestinal infestations play the most important part as predisposing factors.

No theory of the etiology of sprue has been generally accepted though it is probable that more observers are partial to the *yeast* theory than to any other. It seems to have found more supporters in America than abroad. Its inception was in 1901 (Kohlbrugge). Kohlbrugge's yeast was classified as the *Monilia albicans* or the *Oïdium albicans*. It was found in sections of the tongue, the deep strata of the mucosa and portions of the submucosa. Castellani found a number of different yeasts, chief among which were the *Monilia intestinalis*, *M. insolita*, *M. tropica*, *M. fecalis* and *M. enterica*, in the intestinal tract in sprue. The last Castellani regarded as identical with the *Monilia psilosis* of Ashford. Castellani believed that while the yeasts played a part in producing some of the manifestations of sprue, as the frothy stools, they are not to be regarded as the primary cause. Later Bahr (Manson-Bahr) came to the same conclusion. Since 1915 Ashford in Porto Rico has strengthened the mycological conception of the etiology. In 1921 he suggested that there might be the added element of a nutritional deficiency which preceded the sprue infection and prepared the soil for it.

The organism which Ashford regards as the specific etiological factor is thought by him to be separate and distinct from the *Monilia albicans*. Ashford's organism has been named by him *Monilia psilosis*. This yeast is round or slightly oval; its diameter is from 2 to 7 μ; it usually contains a relatively large refractile body and a much larger faintly outlined vacuole. Ashford describes it as a typical member of the monilia group, reproduc-

ing by side buds and terminal conidia from specialized hyphæ, as well as by budding from yeast forms. Ascospores were never seen but chlamydospore-like bodies were frequent, especially in older cultures. There is a tendency to the formation of mycelia which are well developed, usually very abundant and present branching hyphæ. Gas is produced in the presence of maltose, dextrose and levulose always, frequently with saccharose and occasionally with galactose. There is no clouding in the liquid medium by the growth of this organism but there results a considerable sediment. A pellicle is seldom seen but a collar is sometimes produced at the point of contact of the surface of the liquid with the tube. The most rapid production of gas occurs in the dextrose tube, then the levulose tube and lastly in the tube with maltose. The Monilia psilosis is best grown on Sabouraud's agar-agar medium with a hydrogen-ion concentration of about PH 5 or by the phenolphthalein indicator an acidity of 2.5 to 3.5. Owing to the difficulty in preventing the liquefaction of the agar-agar the writer has found it advantageous to make up the acidity with dilute acetic acid. A medium of such acidity will inhibit the growth of practically all bacteria and yet not interfere with the growth of yeasts. Yeasts grow equally as well on the usual media without increased acidity being necessary. The advantage in the high acidity is merely that of inhibition of bacteria. Without this inhibition of bacteria the yeast will not grow satisfactorily if at all. The incubator temperature should be 30° C., thereby inhibiting the bacteria.

In the Philippines L. W. Smith found the same yeast in sprue that Ashford found in Porto Rico and many observers in the United States. The Philippine yeast does not differ from Ashford's description. In differentiating *Monilia psilosis* from *M. albicans* Smith noted that in massive culture after several months the latter still retained a glistening snowy white appearance while the *M. psilosis* had a dirty grayish-yellow or brownish appearance and was much less refractile. The mycelial downgrowth in the medium is much more marked in the *M. psilosis*.

Ashford found the *Monilia psilosis* with ease in sprue during the active stage but in chronic and mild cases it was often quite difficult. During remissions the writer usually does not find the yeast though there are numerous exceptions. In one patient, several years after the last clinical evidence of the disease, the yeast can be grown with ease. In some cases during the height of the process it has been impossible over long periods to secure a growth of the *M. psilosis* though non-pathogenic yeasts might be obtained. In a large series of normal controls the writer has found that the *M. psilosis* occurs in less than 3 per cent. In patients presenting the sore tongue and diarrhœa a positive complement-fixation response may be confidently expected. In this test the antigen is the *M. psilosis* which is autolyzed.

Scott has suggested that sprue may be due to a fault in calcium metabolism. In a series of the writer's cases there has been a notable absence of a deficiency of this sort and Castellani has pointed out that therapy based on this conception is often disappointing.

Pathology.—The fact that the primary lesion of sprue is beneath the epithelium in both the tongue and the intestine, causing superficial des-

quamation, is regarded by some as indicating that whatever the toxic agent may be the action is by the blood rather than as a surface irritant. Castellani says that in the intestine the disease process begins with submucous congestion followed by thrombosis of the vessels and round-cell infiltration; the mucosa suffers because its blood supply is damaged and consequently necrosis results. In somewhat the same manner the œsophagus and stomach suffer. Manson regarded the tongue lesion as a superficial process attended with swelling and congestion of the fungiform papillæ, ulceration, denudation of the surface epithelium and finally by atrophy of the whole tongue.

Many cases have been cited to show that the essential anatomical lesion is ulceration of the small intestine which, if continued long enough, leads to complete atrophy of the villi not unlike that observed in many wasting conditions. This atrophy may be regarded as a natural consequence of a profound nutritional disturbance. Marked decrease in the size of the liver is a part of this atrophic process. The atrophic change of the intestinal tract so often mentioned is not universally present. In Musgrave's cases it was not constant and it was not found by Falconer and Rowe. Baumgartner and Thomas in the autopsy of a case of sprue did not find ulceration of the intestinal tract but were successful in obtaining cultures of the *M. psilosis* from all portions of the tract. These observers noted the presence of enlarged mesenteric lymph nodes which Musgrave also had recorded.

Mayo-Robson found in some cases of sprue postmortem evidence of inflammatory changes of the *pancreas*. In some cases he regarded the disease as chronic pancreatitis rather than sprue. With the frequent deficiency of the pancreatic ferments in sprue, changes in the pancreas are to be expected but the autopsy findings are not uniformly confirmative. Manson mentioned fatty or granular degeneration of acinal cells but did not regard this as more frequent in the pancreas than in the liver or kidney.

Symptoms.—Sprue is a chronic process which makes its appearance so insidiously that it is difficult to obtain an exact account of its duration, or its early course when the patient comes under observation. Usually when first seen the duration is of months and the account of the onset is vague. Short periods of so-called indigestion with brief attacks of sore mouth and tongue, short attacks of diarrhœa lacking any distinctive character and progressive loss of strength usually usher it in. These symptoms may abate and the patient be fairly well for weeks or months but suffers a recurrence which is usually more severe and longer in duration. After months of these vague features which are not distinctive, the more characteristic signs appear.

Usually the first complaint is of sensitiveness of the *tongue* and buccal mucous membrane. At this time the mouth lesion consists merely of a few congested areas on the dorsum or along the edges of the tongue. These areas soon ulcerate and are found not only on the tongue but on the buccal surfaces. Crombie's molar ulcer occurs on the buccal surface opposite the last teeth but cannot be regarded as distinctive of sprue as it has been recorded in pellagra. The fungiform papillæ of the tongue become swollen early and stand out from the surface in a distinctive

fashion. Later there is denudation and large eroded areas may be noted. The tongue is often red-rimmed in a striking way with most of the process limited to this portion. The tongue in sprue has been described as being firm and pointed but it is more often flabby, thereby differing markedly from the firm, pointed tongue of pellagra which latter is of a much deeper shade of red. Salivation is often mentioned and does occasionally occur but it is not comparable to the extreme degree seen usually in pellagra. There is considerable discomfort of the mouth in sprue, especially provoked by hot or acrid foods. Usually this discomfort is not extreme but it may extend into the œsophagus, adding to the objection to the taking of food. The final stage is denudation attended with atrophy of the tongue in some cases. After the subsidence of the attack the tongue usually presents a denuded appearance. In some instances there is a certain degree of fissuring which is superficial and suggests a mild grade of the cobble-stone tongue. A notable feature is the occurrence of attacks of a few days' duration followed by periods of complete remission when there are no subjective indications and few if any objective signs.

Diarrhœa usually occurs early but is not of a distinctive character in the beginning. At first the movements are liquid, bile-stained, rather copious and gradually assume the sprue character. The stool finally is soft rather than liquid and is described as pultaceous. It has been termed the "cow pad" stool because of its marked bovine appearance. The bulkiness is quite notable and suggests the pancreatic type of stool. The amount of feces passed in the twenty-four hours is often startling. One patient stated that during the early hours of the morning the slop jar would be half filled. The color is a light tan with slight variations and the presence of fat is evident from the obvious greasiness. Throughout the fecal mass there is much gas in the form of bubbles. The odor is extremely offensive and the reaction is acid. There is a decided matitudinal character to the diarrhœa, the movements usually starting in the early hours and continuing until early afternoon when temporary subsidence usually occurs. The pale color of the feces is attributed to the excess of unaltered fat and fatty acids. Manson-Bahr says that the normal coloring substance, stercobilin, is present but has undergone reduction, presumably through abnormal bacterial action, into a colorless compound, leukobilirubin, which on oxidation becomes converted into brown pigment. This observer regards the abnormal stools as due to the destruction of the absorbing surface of the ileum and also to the hurrying of the contents of the jejunum through the colon. Much attention has been paid to the loss of fat and nitrogen in the feces. In some of Bahr's cases the utilization of fat was as high as from 70 to 90 per cent. Pratt and Spooner found in 1 case a fat loss of 45 per cent. and a nitrogen loss of 15 per cent. In another case Pratt found a fat loss of 59 per cent. without apparent pancreatic insufficiency and regarded the change in the small intestine as responsible for it. The writer has noted that from day to day there occurs frequently a great variation in the figures.

Great variations in the emptying time of the stomach have been noted and conflicting observations on the analysis of the stomach contents have been recorded. In many cases the free hydrochloric acid is reduced;

in a few it is normal; in a large number there is a complete achylia. When achylia occurs in sprue it is later in the course than is the rule in pernicious anemia. The writer found an absence of free hydrochloric acid in numerous fractions of gastric contents at the height of the disease while the same patient after apparent recovery showed a normal acid content.

Loss of weight is notable and frequent. In 2 cases of the writer's, the patients had lost respectively 100 pounds and 75 pounds.

The *blood* changes are fairly constant and probably more common than the earlier literature indicates. The writer has yet to see a case of sprue in which blood changes did not occur, although in this all observers do not agree. Ashford has stated that the anemia of sprue may approach the pernicious type and that doubt may arise as to its nature. He further states that in some cases it becomes the dominant factor. Manson-Bahr called attention to the close clinical resemblance of some cases of pernicious anemia to sprue especially at the time of onset. L. W. Smith found an anemia resembling pernicious anemia in severity and rapidity of course but showing few of the morphological blood changes of that disease. He thought that it could not be classified as a secondary anemia because of the morphological appearance of the blood cells and the diminution of platelets and of marrow activity. The conclusion reached was that the blood picture was that of the aplastic type and in this numerous other observers are in accord. In a study of megalocytic and non-megalocytic anemia Hampson and Shackle studied the blood in sprue and found the same increase in size noted in Addisonian anemia. In sprue the van den Bergh test for bilirubin in the blood serum gives a positive indirect reaction indicating a so-called hemohepatogenous jaundice. Postmortem study of the tissues in sprue gives a positive reaction to the Perl Prussian-blue test which is regarded as indicating the result of blood destruction consequent on some hemolytic action. In a large series of cases of sprue the color index has been found to be above 1 but not universally so nor throughout the whole course. In most cases while the anemia is of the meglocytic variety there are few normoblasts and still fewer megaloblasts.

Neurological changes have been notably absent in the reports but recently the writer has noted the occurrence of subacute combined degeneration.

Diagnosis.- Sprue has been confused with *pellagra* but there is no occasion for this if it is accepted that pellagra cannot be diagnosed without the presence of, or the definite history of, symmetrical skin lesions. The blood picture in pellagra is lacking; the diarrhœa of sprue is quite distinctive; the changes in the mouth and tongue in the two conditions are readily distinguished. From *pernicious anemia* the diagnosis is much more difficult. Loss of weight, an absence of early achylia and the prominence of a distinctive diarrhœa would seem to make it an easy matter but the writer does not find it so and many diagnoses of sprue at one time have to be revised later and Addisonian anemia substituted. To the diagnosis of Addisonian anemia in certain cases the observer experienced with sprue takes exception.

Prognosis.—Even mild attacks of sprue must be regarded as serious. Many patients are supposed to recover and some probably do but the

criterion of a cure is difficult. The writer recently saw a patient with sprue who was under his care with the same disease eight years before and who had suffered no recurrence in the interval. The course seems to be dependent largely on the early institution of hygienic and dietetic control.

Treatment.—This has advanced little if at all since Manson first advocated rest with a diet of milk and strawberries. The result of the use of strawberries has been so striking that in one clinic this diet is used as a therapeutic test. If there is no improvement the diagnosis of sprue is questioned. However, the strawberry diet has not been universally successful, probably due to the variation in the fruit. The striking results obtained when well-ripened fruit, which has not been forced in a hot house, is used suggest the possibility of some sort of deficiency. Some clinicians in giving milk prefer to remove the cream as the fat digestion in sprue is so faulty. It is important that skimmed milk or whole milk be taken slowly and be given in small amounts at first and be very gradually increased. Some have found that bananas are a satisfactory addition to the milk diet, taking the place of strawberries which cannot always be obtained. The writer has been forced at times to use another diet than milk in certain individuals. The best substitute is the beef diet of Cantlie. Beef without fat or connective tissue is selected, chopped to a fine pulp and quickly cooked in a hot pan on top of the stove. The less cooking the better the result will be. At first a quarter of a pound a day should be taken which is gradually increased to a pound or even more. Nothing else is permitted except hot water. In severe cases it is sometimes better to give the expressed juice of under-done beef in small amounts until improvement is noted.

Probably most important is absolute rest in bed. Long after the symptoms have subsided absolute rest with the restricted diet should be continued, for in no other disease is indiscretion attended so certainly with relapse.

The use of parathyroid gland and calcium lactate, based on the idea of a lowered calcium content of the blood, has been extensively used. In isolated instances brilliant results have been reported. In the writer's cases calcium determinations have shown that all cases of sprue do not present a lowered calcium content and this should be investigated before the treatment is instituted. It is not always successful.

Ashford reports good results from a vaccine made from the *Monilia psilosis*. This yeast is autolyzed at incubator temperature for a week and is killed in the water bath by a temperature of about 70° to 80° C. for one hour. The lower temperature used in the preparation of bacterial vaccines has been found insufficient by the writer. The technique of Michel is satisfactory. A 1 per cent. suspension of the sediment is prepared after five minutes of high speed centrifuging. The initial dose is 0.1 cc. increased by 0.1 cc. each time until 1 cc. is given with an interval of five to seven days.

The writer recovered from pyorrhœal pus of the patient with sprue a yeast of the monilia group which is identical with the Monilia psilosis. If Ashford's work is accepted attention to the hygiene of the mouth

becomes doubly important. One of the few patients apparently well of sprue in this series had all her teeth extracted.

A most important measure is *blood transfusion*. It is in this single particular that the treatment of sprue can be said to have improved.

During convalescence the patient requires the greatest attention for the improvement of weeks can be lost by a single mouthful of improper food. Both in food and in resuming activity the most carefully graduated increases must be made.

References

Ashford, B. K.: *Jour. Am. Med. Assn.*, 1915, **64**, 810; *Am. Jour. Trop. Dis. and Prev. Med.*, 1914, **1**, 32; *Am. Jour. Med. Sci.*, 1915, **150**, 680; *Am. Jour. Med. Sci.*, 1916, **151**, 520; *Am. Jour. Med. Sci.*, 1917, **154**, 157; *Am. Jour. Trop. Med.*, 1922, **2**, 139.

Bahr, P. H.: *Studies in Sprue in Ceylon*, Cambridge Press, 1914.

Falconer and Rowe: *Am. Jour. Trop. Med.*, 1915, **3**, 400.

Fayrer, Sir Joseph: *Trop. Dysentery and Chronic Diarrh.*, London, 1885.

Graham, St. J. B.: *Georgia Practitioner*, 1905, vol. **11**.

Harris, H. F.: *Report of the State Board of Health of Georgia*, 1907.

Manson, Sir Patrick, Allbutt and Rolleston: *A System of Medicine*, vol. **3**, p. 774.

Manson-Bahr, P.: Morbid Anatomy and Pathology of Sprue, *Lancet*, June 7, 1924.

Maumgartner and Thomas: *Clifton Springs Med. Bull.*, 1925, **2**, No. 3

Scott, H. H.: *Lancet*, 1923, ii, 876.

Smith, L. W.: *Jour. Am. Med. Assn.*, 1924, **83**, 1549; *Philippine Jour. Sci.*, 1924, **2**, No. 4.

Wood, E. J.: *Am. Jour. Med. Sci.*, 1915, **150**, 1; *Jour. Am. Med. Assn.*, 1919, **73**, 165; *Southern Med. and Surg. Jour.*, 1922, **86**, 1; *Am. Jour. Med. Sci.*, 1925, **169**, 28; *Southern Med. Jour.*, 1925, **18**, 157.

CHAPTER XII

DISEASES OF THE PANCREAS

By EUGENE L. OPIE, M.D.

GENERAL PATHOLOGY AND SYMPTOMS

Although the pancreas is essential to the normal digestion of proteins, carbohydrates, and fats, and controls the assimilation of carbohydrates, in only a small proportion of cases does disturbance of these functions indicate with certainty disease of the organ. Evidence of disturbed function is obtainable only when the gland is the seat of advanced disease. Complete extirpation of the gland in animals is followed both by glycosuria and by changes in the digestion of proteins and fats; partial extirpation may be unaccompanied by glycosuria or by disturbances of digestion, since a small part of the gland has been found to fulfil both the internal or metabolic and the external or secretory function of the gland. The impairment of function resulting from slight injury may be unrecognizable under ordinary conditions, and demonstrable only by special means which tax the capabilities of the organ. Moreover, complete occlusion of the duct of Wirsung, which is usually the larger duct of the gland, does not necessarily prevent access of the secretion to the intestine, since the duct of Santorini, anastomosing with it, may be large enough to act as an outlet for the entire secretion.

Symptoms Due to Impairment of Pancreatic Secretions.—These concern (1) the external secretion of the gland, indicated by disturbance of digestion or by the effects of retained secretion, and (2) the internal function of the organ, causing disturbance of carbohydrate metabolism.

Incomplete digestion of various elements of the food in association with pancreatic disease is indicated by passage of voluminous feces first noted by Oser. Schmidt determined the weight of the dried feces in individuals receiving a test diet and found that it may be doubled in patients with pancreatic disease. Pratt[1] has made similar observations and has shown that separation of the pancreas from the duodenum may double the weight of the dried feces in dogs receiving a uniform diet.

Pancreatic Enzymes in Duodenal Contents.—The enzymes of the duodenal contents have been studied in normal individuals and in those with pancreatic and other disease, and these studies furnish valuable data for diagnosis of disease of the organ. Crohn,[2] and Chace and Myers[3] found diminution of enzymes in an instance of chronic pancreatitis. Junghans[4] found no enzymes in the duodenal contents in a case of chronic pancreatitis with fatty stools.

[1] *Am. Jour. Med. Sci.*, 1912, **143**, 313.
[2] Ibid., 1913, **145**, 393.
[3] *Arch. Int. Med.*, 1913, **12**, 168.
[4] *Zent. f. d. ges. Physiol. u. Path. d. Stoffw.*, 1911, **6**, 49.

Normal secretion of amylase, trypsin, and lipase was found by Crohn[1] in 103 patients. In 1 case of acute suppurative pancreatitis, in 2 cases of chronic interlobular pancreatitis, one associated with carcinoma demonstrated by autopsy, and in 3 cases, said to be chronic pancreatitis because the head of the pancreas was found swollen at operation, pancreatic enzymes were diminished. They were absent in 2 cases of carcinoma obstructing the pancreatic duct. In 3 cases of epigastric tumor, in 1 in which the nature of the lesion was not determined and in a case of Addison's disease, enzymes were diminished although the pancreas was apparently unchanged.

Concentration of trypsin in duodenal contents has been measured by McClure, Wetmore and Reynolds[2] in terms of non-protein nitrogen obtained by digestion of casein solution. Amylolytic activity has been estimated in milligrams of glucose produced by action of a measured quantity of duodenal contents on a solution of starch. Lipolytic enzyme has been measured by the action of duodenal contents on an emulsion of cottonseed oil. Normal concentration of enzymes was found with acute and chronic lesions of the pancreas which did not involve the head of the gland, for example, carcinoma of the tail. Low concentrations were found with destructive lesions, such as carcinoma of the head of the pancreas and acute pancreatic necrosis, and with chronic pancreatitis with or without extensive alteration of the glandular parenchyma. Low concentration of one or two enzymes with normal concentration of the other (dissociated concentration) was found in patients convalescing from acute pancreatic necrosis. With disease of the biliary tract, enzymes were normal when there was no obstruction of the pancreatic ducts but abnormally low or dissociated concentration was present when an obstruction of the common duct occluded the pancreatic duct as well.

Enzymes of duodenal contents appear to furnish a more accurate index of pancreatic disease than changes in the feces. Impaired digestion has uncertain significance in the presence of biliary obstruction or in association with intestinal disease which retards absorption. Crohn found instances in which enzymes were present in normal concentration in the duodenal contents but absent in the feces.

Steatorrhœa.—Although regarded by Friedreich and other writers of much diagnostic value, they recognized the fact that it accompanies only a small proportion of even grave pancreatic disorders. Finding jaundice associated with cases of pancreatic disease, in which steatorrhœa indicated impaired absorption of fat, Fr. Müller attributed the symptom to obstruction of the common bile duct. A review of recorded instances of steatorrhœa with pancreatic disease, made by Fitz[3] in 1903, does not confirm this view, but establishes the diagnostic value of the symptom in the relatively small number of cases in which it occurs. In 17 instances of steatorrhœa in which jaundice was absent the lesion of the pancreas was in 7 cases tumor, usually cancer; in 6 cases calculi within the ducts; in 2 cases cysts with atrophy; in 2 instances the lesion was designated fatty degeneration.

[1] *Arch. Int. Med.*, 1915, **15**, 581.
[2] Ibid., 1921, **27**, 706; *Am. Jour. Med. Sci.*, 1924, **167**, 649.
[3] *Transactions of the Congress of American Physicians and Surgeons*, 1903, **6**, 36.

In the recorded cases the character of the feces has varied considerably. In some instances superficial examination demonstrates the presence of free fat, which is described as oily or like butter, while in other cases the feces are described as gray, silvery gray, or asbestos-like. The fat, which is liquid when passed, may solidify on cooling and form a layer covering the fecal mass. The presence of fat recognizable by the eye constitutes a true steatorrhœa.

In the uniform metallic-gray or asbestos-like stools sometimes seen, the abnormal fatty contents are demonstrated with greater certainty by chemical methods which may show the amount of neutral fat, fatty acids, and soaps. Such fatty stools may occur in normal individuals who have ingested fat in quantity so great that the normal limit of absorption has been exceeded. Ability to digest and absorb fat is diminished, according to Nothnagel, when bile fails to enter the intestine, when absorption is hindered by certain diseases of the intestine or its lymphatic apparatus—namely, amyloid disease, extensive atrophy of the mucous membrane, caseation of the mesenteric lymphatic glands, and tuberculous peritonitis, or when very active peristalsis prevents the normal action of the digestive juices.

Experimental study of fat absorption after ligation of pancreatic ducts has given conflicting results. Lombroso has maintained that ligation alone causes little increase of eliminated fat, although complete extirpation of pancreatic tissue is followed by elimination of all ingested fat. Since the presence of a viable subcutaneous graft has served to increase fat absorption Lombroso has assumed that pancreatic enzymes may reach the intestine even though there is no communication between pancreas and duodenum. One group of observers confirmed these observations and another group contradicted them. Pratt, Lamson and Marks[1] found deficient fat absorption in 5 dogs in which after ligation of ducts omentum was inserted between the intestine and the cut end of the pancreas. In patients with pancreatic disease Crohn found that ingested fat was not eliminated in abnormal amount with the feces, even though the duodenal contents contained no pancreatic enzymes and thinks that the gland aids absorption even though it does not communicate with the duodenum.

In healthy individuals from 12 to 16 per cent. of ingested fat is eliminated with the feces (Schmidt and Strassburger[2]). With obstructive jaundice loss of fat is increased to from 20 to 30 per cent. In 5 cases with closure of the pancreatic duct, collected from the literature by Crohn, fat elimination varied from 19.7 to 73 per cent., the average being 67.3 per cent. In 19 cases of chronic pancreatitis, accompanied by jaundice in only 2 cases, fat loss varied from 18 to 72 per cent., the average being 39.3 per cent. In 15 cases of carcinoma of the pancreas, with few exceptions accompanied by jaundice, fat loss was from 18 to 85 per cent., the average being 62.3. These observations were made upon instances of advanced pancreatic diseases and give no information concerning absorption in the presence of early changes in the gland.

[1] *Trans. Assn. Am. Phys.*, 1909, **24**, 266.
[2] *Die Feces des Menschen*, Berlin, 1905.

By administering fresh pancreas to animals from which the pancreas has been removed the consequent impairment of fat absorption has been diminished. Abelmann found that the pancreas of the pig fed to a dog, the pancreas of which had been extirpated, caused a decrease in the amount of undigested fat and of protein as well in the feces. Similar observations have been made by other experimenters, and are confirmed by a few observations upon patients with pancreatic disease. Fles, quoted by Friedreich, records the case of a man suffering with diabetes mellitus who passed undigested meat and fat in such quantities with the feces that it could be separated by ounces. A part of the milky fluid obtained by rubbing in a mortar one-half of the fresh pancreas of a calf with 6 ounces of water and straining the mixture was administered after each meal in such quantity that one pancreas was consumed daily. At the end of two days all fat had disappeared from the feces and the number of undigested fibres of striped muscle was greatly diminished. Whenever the administration of the infusion was discontinued, fat and muscle fibres reappeared in the feces. The condition of the patient improved for a time, but diabetes mellitus persisted, and death occurred as the result of tuberculosis. Advanced sclerosis of the pancreas was found at autopsy. In a patient with jaundice and suspected cancer of the pancreas Oser observed improved digestion of fats following the administration of 1 gm. of pancreatin taken daily in divided doses. Tileston[1] collected the published cases in which the effect of pancreas or pancreatic preparations upon absorption was studied in patients with pancreatic disease and found that loss of both fat and nitrogen may be decreased.

Little is known concerning the effect of continued steatorrhœa upon nutrition and health. Walker has described the case of a man who for twenty years passed large colorless stools of putrid odor, containing free oily or solid fat. There was no jaundice. During this time he was in good health and engaged in the practice of medicine; there was no marked emaciation. He died at the age of ninety years. The pancreas was apparently replaced almost wholly by fat, and its duct was occluded by an irregular calculus situated about an inch from the duodenum.

Azotorrhœa.—The presence of undigested protein material in the feces, so-called azotorrhœa, has been less frequently observed in association with pancreatic disease than disturbed digestion of fat. After causing almost complete destruction of the pancreas in dogs, Claude Bernard found undigested muscle fibres and even large pieces of meat in the feces. Abelmann found that less than 2 per cent. of the nitrogen of the food reappears in the feces of normal dogs; when the pancreas is completely removed, 56 per cent. of ingested nitrogen was lost with the feces, whereas after partial removal 46 per cent. was lost. When the pancreas of the pig was administered, loss of nitrogenous material was diminished to approximately 24 per cent. Other observers have obtained similar results. In a case described by Wientraub autopsy demonstrated advanced chronic interstitial pancreatitis; in the feces during life he recovered 45.2 per cent. of the ingested protein and only 22.2 per cent. of the fat taken as food. He suggests that pancreatic disease causes as

[1] *Trans. Assn. Am. Phys.*, 1911, **26**, 537.

great disturbance of the digestion of proteins as of fats, perhaps an even greater disturbance, and is therefore distinguishable from intestinal disturbances such as amyloid disease, caseation of the mesenteric lymph glands, etc., which hinder absorption of fat alone.

In healthy individuals from 4 to 6 per cent. of the nitrogen ingested with the food is recoverable in the feces (Schmidt and Strassburger). With closure of the pancreatic duct Zoja recovered 70 per cent., Pratt and Morrison 50.9, Harley 40, and Brugsch 2.54 per cent. Crohn collected from the literature 12 cases of chronic pancreatitis in which nitrogen elimination varied from 30.4 to 69 per cent., the average being 46.3 per cent. With tumor of the pancreas elimination in 11 instances varied from 14.5 to 41 per cent., the average being 28.6 per cent. Occlusion of the common bile duct associated with jaundice does not diminish the digestion of protein and does not increase the elimination of nitrogenous products by way of the feces.

The presence of undigested meat in the feces may give indication of disturbed protein digestion. Fles found well-preserved muscle fibres in the feces of the patient previously mentioned, and administration of an extract made from the pancreas of a calf caused their disappearance. Fitz collected from the literature only 8 cases in which the presence of undigested muscle fibres in the feces had been associated with clearly demonstrated pancreatic disease; in 5 of these cases steatorrhœa was present. The condition, as he pointed out, probably occurs only when there is extreme diminution of the pancreatic juice, and is significant only when gastric digestion is normal, when the diet contains no excess of meat, and where there is no diarrhœa.

The *persistence of nuclei in remnants of muscle fibres passed with the feces* was proposed by Adolph Schmidt as a test of the efficiency of pancreatic digestion. He has maintained that the nuclear material of meat can be digested only by the pancreatic juice but in a patient with total absence of pancreatic enzymes in the duodenal contents, Atchley[1] found the usual urinary elimination of purin bases after administration of food (thymus) rich in nuclear material. Steele[2] found the test little more than an index of proteolytic digestion in the intestine.

Methods for demonstrating the presence of trypsin in the feces are of little if any value. Pratt[3] found no trypsin in the feces in 4 normal individuals and Tileston[4] had the same result in 7 instances.

Impaired Digestion of Starch.—Methods for determination of quantitative variations in the activity of diastase in the urine and feces were proposed by Wohlgemuth and by Wynhausen and have been widely used in the effort to find a measure of pancreatic deficiency. Diastase requires no activator and with the exception of that secreted by the salivary glands is formed almost exclusively by the pancreas. Several observers have found increase of diastase in the urine and decrease in the feces in association with conditions which obstruct the outflow of pancreatic juice. T. R. Brown using milk diet, a purgative and precise precautions in collecting and testing specimens found that the fecal diastase

[1] *Arch. Int. Med.*, 1915, **15**, 654.
[2] *University of Pennsylvania Medical Bulletin*, 1906, vol. **19**.
[3] *Am. Jour. Med. Sci.*, 1912, **143**, 314.
[4] *Arch. Int. Med.*, 1912, **9**, 535.

By administering fresh pancreas to animals from which the pancreas has been removed the consequent impairment of fat absorption has been diminished. Abelmann found that the pancreas of the pig fed to a dog, the pancreas of which had been extirpated, caused a decrease in the amount of undigested fat and of protein as well in the feces. Similar observations have been made by other experimenters, and are confirmed by a few observations upon patients with pancreatic disease. Fles, quoted by Friedreich, records the case of a man suffering with diabetes mellitus who passed undigested meat and fat in such quantities with the feces that it could be separated by ounces. A part of the milky fluid obtained by rubbing in a mortar one-half of the fresh pancreas of a calf with 6 ounces of water and straining the mixture was administered after each meal in such quantity that one pancreas was consumed daily. At the end of two days all fat had disappeared from the feces and the number of undigested fibres of striped muscle was greatly diminished. Whenever the administration of the infusion was discontinued, fat and muscle fibres reappeared in the feces. The condition of the patient improved for a time, but diabetes mellitus persisted, and death occurred as the result of tuberculosis. Advanced sclerosis of the pancreas was found at autopsy. In a patient with jaundice and suspected cancer of the pancreas Oser observed improved digestion of fats following the administration of 1 gm. of pancreatin taken daily in divided doses. Tileston[1] collected the published cases in which the effect of pancreas or pancreatic preparations upon absorption was studied in patients with pancreatic disease and found that loss of both fat and nitrogen may be decreased.

Little is known concerning the effect of continued steatorrhœa upon nutrition and health. Walker has described the case of a man who for twenty years passed large colorless stools of putrid odor, containing free oily or solid fat. There was no jaundice. During this time he was in good health and engaged in the practice of medicine; there was no marked emaciation. He died at the age of ninety years. The pancreas was apparently replaced almost wholly by fat, and its duct was occluded by an irregular calculus situated about an inch from the duodenum.

Azotorrhœa.—The presence of undigested protein material in the feces, so-called azotorrhœa, has been less frequently observed in association with pancreatic disease than disturbed digestion of fat. After causing almost complete destruction of the pancreas in dogs, Claude Bernard found undigested muscle fibres and even large pieces of meat in the feces. Abelmann found that less than 2 per cent. of the nitrogen of the food reappears in the feces of normal dogs; when the pancreas is completely removed, 56 per cent. of ingested nitrogen was lost with the feces, whereas after partial removal 46 per cent. was lost. When the pancreas of the pig was administered, loss of nitrogenous material was diminished to approximately 24 per cent. Other observers have obtained similar results. In a case described by Wientraub autopsy demonstrated advanced chronic interstitial pancreatitis; in the feces during life he recovered 45.2 per cent. of the ingested protein and only 22.2 per cent. of the fat taken as food. He suggests that pancreatic disease causes as

[1] *Trans. Assn. Am. Phys.*, 1911, **26**, 537.

great disturbance of the digestion of proteins as of fats, perhaps an even greater disturbance, and is therefore distinguishable from intestinal disturbances such as amyloid disease, caseation of the mesenteric lymph glands, etc., which hinder absorption of fat alone.

In healthy individuals from 4 to 6 per cent. of the nitrogen ingested with the food is recoverable in the feces (Schmidt and Strassburger). With closure of the pancreatic duct Zoja recovered 70 per cent., Pratt and Morrison 50.9, Harley 40, and Brugsch 2.54 per cent. Crohn collected from the literature 12 cases of chronic pancreatitis in which nitrogen elimination varied from 30.4 to 69 per cent., the average being 46.3 per cent. With tumor of the pancreas elimination in 11 instances varied from 14.5 to 41 per cent., the average being 28.6 per cent. Occlusion of the common bile duct associated with jaundice does not diminish the digestion of protein and does not increase the elimination of nitrogenous products by way of the feces.

The presence of undigested meat in the feces may give indication of disturbed protein digestion. Fles found well-preserved muscle fibres in the feces of the patient previously mentioned, and administration of an extract made from the pancreas of a calf caused their disappearance. Fitz collected from the literature only 8 cases in which the presence of undigested muscle fibres in the feces had been associated with clearly demonstrated pancreatic disease; in 5 of these cases steatorrhœa was present. The condition, as he pointed out, probably occurs only when there is extreme diminution of the pancreatic juice, and is significant only when gastric digestion is normal, when the diet contains no excess of meat, and where there is no diarrhœa.

The *persistence of nuclei in remnants of muscle fibres passed with the feces* was proposed by Adolph Schmidt as a test of the efficiency of pancreatic digestion. He has maintained that the nuclear material of meat can be digested only by the pancreatic juice but in a patient with total absence of pancreatic enzymes in the duodenal contents, Atchley[1] found the usual urinary elimination of purin bases after administration of food (thymus) rich in nuclear material. Steele[2] found the test little more than an index of proteolytic digestion in the intestine.

Methods for demonstrating the presence of trypsin in the feces are of little if any value. Pratt[3] found no trypsin in the feces in 4 normal individuals and Tileston[4] had the same result in 7 instances.

Impaired Digestion of Starch.—Methods for determination of quantitative variations in the activity of diastase in the urine and feces were proposed by Wohlgemuth and by Wynhausen and have been widely used in the effort to find a measure of pancreatic deficiency. Diastase requires no activator and with the exception of that secreted by the salivary glands is formed almost exclusively by the pancreas. Several observers have found increase of diastase in the urine and decrease in the feces in association with conditions which obstruct the outflow of pancreatic juice. T. R. Brown using milk diet, a purgative and precise precautions in collecting and testing specimens found that the fecal diastase

[1] *Arch. Int. Med.*, 1915, **15**, 654.
[2] *University of Pennsylvania Medical Bulletin*, 1906, vol. **19**.
[3] *Am. Jour. Med. Sci.*, 1912, **143**, 314.
[4] *Arch. Int. Med.*, 1912, **9**, 535.

strate insufficiency of pancreatic digestion in a much larger number of instances of duct obstruction at a time when diabetes has not appeared.

Histological studies explain the relationship of a variety of diseases, such as arteriosclerosis and cirrhosis of the liver, to diabetes mellitus. Grube found arteriosclerosis 66 times among 117 cases of diabetes. Chronic interstitial pancreatitis accompanying sclerosis of the pancreatic vessels has been described; this change which affects the interacinar tissue of the gland implicates the island of Langerhans. G. Hoppe-Seyler,[1] who studied 18 such cases, found a close relation between the severity of the glycosuria and the degree of change affecting the islands of Langerhans. The frequency with which diabetes is caused by disease of the arteries is shown by 112 cases of diabetes which have been collected from the literature; in association with general arteriosclerosis there was, in 23 cases, sclerosis of the pancreatic arteries and interacinar pancreatitis; in 26 additional cases there was either general or local arterial sclerosis, in 10 instances with interacinar pancreatitis.

The frequency with which diabetes mellitus accompanies *cirrhosis of the liver* has been explained by the presence of chronic pancreatitis. Conditions which cause cirrhosis of the liver act upon the pancreas and cause chronic inflammation. There are numerous instances of this association, which is well exemplified by hemochromatosis; pigmentary cirrhosis of the liver is accompanied by chronic pancreatitis, which invades the islands of Langerhans and causes diabetes.

That *alimentary glycosuria* demonstrable by the administration of a fixed quantity of sugar may accompany a variety of pancreatic lesions is shown by the investigation of Wille. From 70 to 100 gm. of grape sugar were administered in the morning before other food had been taken to 800 patients suffering with a great variety of diseases. Subsequently 77 of them came to autopsy. Temporary glycosuria had been produced in 15 of these, and grave lesions of the pancreas were found in 10—namely, chronic interstitial inflammation, or carcinoma of the gland, either primary or secondary to tumors in the stomach, liver, or gall-bladder. Alimentary glycosuria may occur in the absence of demonstrable pancreatic disease. Its occurrence, however, may give information when other conditions suggest the presence of pancreatic disease of moderate intensity. Hoppe-Seyler tested the ability of individuals with arteriosclerosis to assimilate 100 gm. of glucose. Alimentary glycosuria was present in 42 per cent. of 62 patients with arteriosclerosis, and was more frequently observed when arteriosclerosis was associated with acute alcoholism.

Retarded Development with Pancreatic Disease in Children.—So-called *infantilism* has been associated with pancreatic lesions. Bramwell described a case in which in association with diarrhœa there was from the eleventh to the eighteenth year retarded physical development. Administration of glycerin extract of pancreas was followed by disappearance of the diarrhœa and rapid increase of weight. Thompson described 2 cases with diarrhœa, a man aged twenty-four and a boy aged eighteen

[1] *Deutsches Arch. f. klin. Med.*, 1904, **81**, 119.

years who had the appearance of children of ten and of nine years respectively; improvement followed the use of pancreatic extract. Rentoul described an instance of the same kind. In the case of Langdon-Brown, a boy, aged sixteen years, with the appearance of a child of eight suffered with congenital syphilis and fatty diarrhœa; chronic pancreatitis regarded as syphilitic was found at autopsy. Clarke and Hadfield[1] described an instance of congenital pancreatic disease with infantilism in a boy aged four years. He had the appearance of a child of two years and the height of a child of three years. There had been fatty diarrhœa but no glycosuria. Death occurred from bronchopneumonia and autopsy showed that the pancreas was represented by a mass of fat (lipomatosis) within which there was pancreatic tissue representing about one-twentieth of the normal gland.

FAT NECROSIS

This lesion, characterized by the death of fat cells in sharply circumscribed areas, is frequently associated with disease of the pancreas. The lesion when widely disseminated is, in the greater number of instances, the result of acute hemorrhagic pancreatitis. Its recognition is of great importance, since the characteristic opaque white foci studding the abdominal fat explain the nature of an otherwise obscure condition.

Etiology.—The inconstant results of bacteriological examinations do not support the opinion of a few observers (Ponfick) who have maintained that the lesion is caused by bacteria. Its relation to bacteria is doubtless that suggested by Welch, who obtained the colon bacillus from foci of fat necrosis in association with hemorrhagic pancreatitis; diphtheritic and ulcerative colitis apparently had facilitated the entrance of *Bacillus coli*, which were found not only in the patches of necrotic fat but in the mesenteric lymph glands, liver, bile, lungs, spleen, and kidneys.

Experimental Fat Necrosis.—Studies of R. Langerhans first brought the lesion into relation with the peculiar physiology of the pancreas. He demonstrated that the fat of the necrotic cell is split into fatty acids, which are deposited as needle-like crystals, and glycerin which is absorbed. The occurrence of the lesion in association with disease of the pancreas, its greatest intensity in the neighborhood of the gland, and the changes demonstrable within the fat cells suggested the probability that the pancreatic ferments, particularly the fat-splitting ferment, have an important part in its production. Hildebrand and Dittmer subjected the pancreas to a variety of injuries and produced fat necrosis. If the gland were simply cut across, thus allowing the escape of the pancreatic secretion foci of necrosis were found in the immediate neighborhood. If penetration of pancreatic secretion into fat tissue is facilitated by transplanting the duodenal part of the pancreas containing the severed ends of the ducts into the subcutaneous fat of the abdominal wall in cats, extensive subcutaneous necrosis of fat is thus produced (Opie). In these experiments conditions were present which afford an opportunity for the escape of pancreatic secretion into the tissue surrounding the gland.

[1] *Quar. Jour. Med.*, 1923–1924, **17**, 358.

Flexner demonstrated the presence in the necrotic foci of a ferment capable of splitting neutral butter fat and setting free acids which are recognizable by suitable tests. That the lesion is caused by a ferment is further shown by the experiments of Wells;[1] watery extracts of the pancreas of the hog constantly produce fat necrosis in cats and dogs, but fail to do so when boiled or after heating to a temperature above 71° C. Whether the lesion is wholly due to the action of the fat-splitting ferment or is the result of its action on tissue previously injured by some other constituent of the pancreatic juice, perhaps by the proteolytic ferment, is not definitely determined.

Incidence of Fat Necrosis.—In human cases extensive fat necrosis is more frequently associated with hemorrhagic and gangrenous pancreatitis than with other lesions of the gland, and constantly accompanies acute hemorrhagic pancreatitis produced experimentally by the introduction of a great variety of irritant substances into the gland. The fact that bile forms a favorable medium for the action of the pancreatic ferments, and particularly of the fat-splitting ferment, the activity of which may be increased by it twofold or threefold, probably explains in part the extent of the lesion accompanying many cases of hemorrhagic pancreatitis which may be caused by the penetration of bile into the pancreas. Fat necrosis has been found with obstruction of the duct of Wirsung caused by pancreatic calculi, by biliary calculi, or by carcinoma invading the head of the pancreas, but in such cases foci of necrosis are not abundantly distributed, nor does the lesion usually follow obstruction of the pancreatic duct. In a small proportion of cases chronic interstitial pancreatitis is accompanied by fat necrosis, probably caused by constriction of small branches of the pancreatic duct.

In several cases of extensive fat necrosis no noteworthy lesion of the pancreas has been demonstrable. In such a case described by Fraenkel the lesion was explained by a gall-stone lodged in the diverticulum of Vater, while in a somewhat similar case of Flexner's, gall-stones were present in the common bile duct near its termination. A unique case described by Wulff[2] is not in accord with other observations and with present knowledge of the lesion is unexplainable, unless an incomplete autopsy failed to disclose an aberrant pancreas, biliary calculi, or some cause of duct obstruction.

Pathological Anatomy.—A feature of the lesion is its occurrence in sharply defined foci. On opening the abdomen the omentum and perhaps fat in other situations is found to be studded with rounded or oval areas, which vary in diameter from less than one to five or more millimeters. They are very conspicuous, on account of their opaque, white or yellowish color, in sharp contrast with the translucent golden yellow of the fat in which they occur. These areas are not infrequently surrounded by a narrow hemorrhagic zone. Such foci are most numerous upon the peritoneal surface, usually extending only a short distance below it, but also occur embedded in the fat. Particularly in the neighborhood of the pancreas, where they are most numerous, foci of necrosis may be

[1] *Jour. Med. Research*, 1903, **9**, 70.
[2] *Berliner klin. Wchnschr.*, 1902, **39**, 734.

large and confluent, giving a tallow-like whiteness to extensive areas of fat. Discrete foci in greater or less number may stud the perinephritic fat, the mesocolon, the mesentery, and the omentum. Foci of necrosis occur less frequently below the parietal peritoneum and upon the surface of the diaphragm.

In some instances fat necrosis has extended beyond the peritoneal cavity. Hansemann has twice seen foci of necrosis in the subcutaneous fat, while in severeal instances the fat of the pericardial and pleural cavities has been implicated. Chiari has described a remarkable instance of widespread fat necrosis. Gangrenous pancreatitis had caused such complete disintegration of the gland that the duct of Wirsung was eroded and communicated directly with the cavity of the bursa omentalis; areas of the fat necrosis, often the size of a pea, were present about the lesser peritoneal cavity, in the mesentery, in the subperitoneal fat of the abdominal wall, in the subpericardial and subpleural fat, and in the subcutaneous tissue.

Microscopic examination of the foci of necrosis shows that the cells, of which the outlines are still preserved, although the nuclei have disappeared, contain at an early stage crystals of fatty acid. Calcium salts combine with these fatty acids to form calcium salts readily demonstrable by microchemical reactions. A few polynuclear leukocytes find their way into the necrotic tissue, but when numerous their presence is due to secondary infection. According to Wells the lesion experimentally produced may be recognizable three hours after the application of pancreatin to fat. Proliferation of fixed tissue cells occurs in the periphery of the necrotic area. The lesion may so completely disappear that its site is no longer recognizable. Wells found fat necrosis in a dog of which the abdomen was opened four days after the injection of pancreatin, but seven days later the lesion had completely disappeared. In a case of acute cholecystitis Körte found at operation typical areas of fat necrosis; the patient recovered, but at a second operation, undertaken a year later for the relief of symptoms suggesting the presence of a gallstone in the common bile duct, foci of necrosis were no longer present.

Clinical Significance of Fat Necrosis.—These facts demonstrate that the lesion is caused by pancreatic juice diverted from its proper channels into the tissues about the gland. When the outflow of bile is obstructed, the bile dammed back upon the liver reaches the interstitial tissue of the gland, and hence is transported to all parts of the body. When the secretion of the pancreas, likewise dammed back upon the gland, reaches the interstitial tissue of the organ, and hence, probably by way of the tissue spaces finds its way into tissues at some distance from the gland, its presence is not indicated by any colored constituent. Focal fat necrosis is in such case the only readily recognizable effect of the aberrant secretion, and for diagnosis of pancreatic disease is available only to the surgeon who opens the abdomen. Hansemann has mentioned a unique case in which circumscribed areas of cutaneous injection marked the site of foci of necrosis shown by postmortem examination to be situated in the subcutaneous tissue of the abdominal wall, but rarely does the characteristic lesion implicate fat outside of the abdominal cavity.

Since disseminated foci of fat necrosis indicate in most instances acute hemorrhagic or gangrenous pancreatitis, its recognition at operation is of great importance. By those who have not previously seen the lesion it may be mistaken for caseous miliary tubercles or for carcinomatous nodules which have undergone necrosis, but the absence of elevation or other evidence of newly formed tissue shows that necrosis has affected the fat.

Since abundant evidence has shown that fat necrosis is due to the action of the fat-splitting ferment secreted by the pancreas, the possibility suggests itself that the ferment which is free in the tissues may be excreted by the kidneys. Recognition in the urine of a fat-splitting ferment derived from the pancreas would afford means for the diagnosis of obscure pancreatic disease accompanied by fat necrosis. With the urine removed at autopsy from the bladder of an individual dead with acute hemorrhagic pancreatitis and fat necrosis, the writer obtained a reaction which indicated the presence of the fat-splitting ferment. The method of identifying this enzyme was that described by Kastle and Loevenhart, who showed that the presence of fat-splitting ferment may be demonstrated by use of ethyl butyrate. Experiments of Hewlett[1] show that a variety of injuries to the pancreas of dogs is followed by the appearance in the urine of a ferment which is capable of decomposing ethyl butyrate into butyric acid and alcohol. Very little if any of such ferment is present in the normal urine; after obstruction of the pancreatic duct he found it during a period of from three to five days, but it is present in greatest amount as the result of experimental hemorrhagic pancreatitis. The method which Hewlett describes in detail can be used to examine the urine when pancreatic disease with fat necrosis is suspected.

HEMORRHAGIC NECROSIS OF THE PANCREAS

The Middleton-Goldsmith Lecture of Fitz, published in 1889, contains a classification of acute pancreatic diseases which served as a basis for the first accurate description of their symptomatology. He found that acute inflammation of the gland may be hemorrhagic, gangrenous, or suppurative. His description of the symptomatology of so-called acute hemorrhagic pancreatitis has made typical instances of the condition recognizable during life. Gangrenous pancreatitis, according to Fitz, although it may follow other conditions, is usually the result of the hemorrhagic lesion. Suppurative pancreatitis resembles suppurative inflammation of other organs. Fitz noted the relationship of so-called fat necroses to acute pancreatic disease, already suggested by Chiari, and found that it more frequently accompanied hemorrhagic and gangrenous than suppurative inflammation.

Suppurative pancreatitis does not differ from similar lesions of other organs and is described in a special section (page 681). Study of the changes which occur with the hemorrhagic and gangrenous lesions of

[1] *Jour. Med. Research*, 1904, **11**, 377.

the gland shows that necrosis is the underlying change. Inflammation is absent at the onset of the disease and the designation hemorrhagic necrosis of the pancreas is preferable to acute hemorrhagic pancreatitis. Experimental studies have shown that the lesion with all the characters which occur in man, can be reproduced in animals by a variety of irritants which produce necrosis of the pancreatic parenchyma. Necrosis implicating the walls of bloodvessels is accompanied by hemorrhage and at the margin of the necrotic tissue there is accumulation of inflammatory products. The condition described as gangrene, characterized by discoloration and softening of necrotic tissue infiltrated with blood, represents a late stage of the same lesion.

Pancreatic Hemorrhage.—Those who have systematically described diseases of the pancreas have given special consideration to so-called *pancreatic apoplexy* or hemorrhage into the pancreas; the condition has medicolegal interest, since it is believed to be one of the causes of sudden death. Hemorrhage into the substance of the gland may be caused by traumatism, or by malignant growth, and minute extravasations may be associated with various infectious diseases; such hemorrhage presents nothing peculiar to the organ. The literature contains numerous cases in which a hemorrhagic lesion of the gland has been the only explanation of the rapidly fatal illness of an apparently healthy individual. In some cases cited as examples of pancreatic hemorrhage, as Seitz explains, it is improbable that the pancreatic lesion has been the cause; whereas, in other cases, such as those described by Reubold and Rehm, after poisoning with morphine, after strangling, or after hemorrhage from the femoral vein, the amount of blood in and about the gland has been so small that it may be referred to the hemorrhagic extravasation which Chiari has described in association with postmortem or agonal self-digestion.

Numerous cases have demonstrated that extensive hemorrhage into the peripancreatic tissues may occur with so-called hemorrhagic pancreatitis; necrosis is primary, and the hemorrhage and inflammation are its consequences. When both inflammation and hemorrhage coexist, the difficulty of deciding which preceded the other is obviously great, for an accumulation of blood in and about the duodenum would quickly become the seat of bacterial infection, and an abscess cavity would be formed. The existence of hemorrhage without evidence of inflammation has been believed to demonstrate the occurrence of so-called apoplexy. Atheroma of arteries and fatty degeneration of the pancreatic parenchyma, cited as causes of hemorrhage, have been found in only a limited number of cases. Knowledge of the pathology of hemorrhagic necrosis of the pancreas has facilitated the description of such cases, and the literature of recent years contains few, if any, instances of so-called apoplexy. An instance of pancreatic hemorrhage is described by Simpson. The pancreas was the seat of hemorrhagic infiltration and the organ was surrounded by semifluid clotted blood. In view of subsequent observations the presence of a gall-stone lodged at the orifice of the common bile duct leaves little doubt that this case is a typical example of hemorrhagic necrosis.

Etiology.—Hemorrhagic necrosis of the pancreas occurs more frequently in men than in women. Among 41 instances of the hemorrhagic lesion Körte found 37 were in males and 4 in females; in 40 cases of so-called gangrenous pancreatitis, 21 were in males and 19 in females. The disease appears to have a more rapidly fatal course in men than in women. Of 121 cases of hemorrhagic and gangrenous pancreatitis cited by Peiser,[1] 79 were in males and 42 in females. The greater number of cases occur between the ages of twenty and fifty years.

A variety of conditions has been believed to favor the disease. Individuals in apparent good health are not infrequently attacked; those with abundant adipose tissue are said to be specially susceptible. About half the cases of hemorrhagic and of gangrenous pancreatitis, Fitz found, are preceded by attacks of indigestion, accompanied by pain either referred to the region of the stomach or believed to be biliary colic.

From the hemorrhagic pancreas and from the associated foci of fat necrosis, a variety of *bacteria*, in many instances *Bacillus coli*, has been isolated, but according to almost all observers the results of bacteriological examination, which have been very inconstant, indicate that the various organisms bear no etiological relation to the disease and are secondary invaders. The acutely inflamed gland may contain no bacteria.

There is no evidence to support the suggestion that the lesion is caused by infection transmitted from the biliary passages to the pancreas by way of the lymphatics.

Experiments of Hlava have shown that the lesion of acute hemorrhagic pancreatitis can be reproduced by injecting artificial gastric juice into the pancreatic ducts of dogs. The lesion which has followed the introduction of cultures of *Bacillus coli*, *Bacillus lactis aërogenes*, and *Bacillus capsulatus* of Friedländer, the same writer attributed to the acid products of these organisms. Carnot reproduced the lesion by injecting diphtheria toxin, and Flexner used weak solutions of hydrochloric, nitric, and chromic acids, sodium hydroxide, and formalin.

Hemorrhagic Necrosis and Cholelithiasis.—The writer[2] has described a mechanism by which bile may be diverted from the bile passages into the pancreatic duct and has shown that bile injected into the pancreatic duct of animals causes typical hemorrhagic necrosis of the pancreas with disseminated fat necrosis. A corpulent man, aged forty-eight years, who had suffered with attacks of indigestion was suddenly seized with severe pain in the abdomen accompanied by nausea. The pain diminished in severity but two days before death returned with its former intensity. At autopsy widely disseminated fat necrosis was found and the much enlarged pancreas had an almost uniform reddish-black color. A small gall-stone (3 mm. in diameter) had lodged firmly at the orifice of the diverticulum of Vater (which was 10 mm. in length with an orifice 1 mm. in diameter) so that it had converted the common bile duct and the duct of Wirsung into a continuous closed channel from which neither bile nor pancreatic juice could escape. The pancreatic duct and its larger

[1] *Deutsche Ztschr. f. Chir.*, vol. **65**.

[2] *Johns Hopkins Hosp. Bull.*, 1901, **19**, 182.

branches were stained bright green with bile. Bacteriological examination of the hemorrhagic pancreas gave negative results. Experiments of the writer showed that 5 cc. of bile from one dog injected into the pancreatic duct of another was followed by hemorrhagic necrosis fatal within twenty-four hours. Flexner found that the ability of bile to cause hemorrhagic necrosis is attributable to the bile salts.

Nordmann claimed that bile alone will not produce hemorrhagic pancreatitis for he found none when bile, as he believed, was diverted into the pancreatic duct of dogs by a purse-string ligature placed about the common duodenal orifice of bile and pancreatic ducts. When after the same operation a suspension of intestinal bacteria was introduced into the gall-bladder pancreatitis with fat necrosis followed. Archibald[1] obtained experimental evidence that bacteria may have a part in the production of pancreatic necrosis. Mann and Giordano placed a ligature about the common bile duct of the goat, midway between its duodenal end and its junction with the pancreatic duct, and found that no pancreatic necrosis occurred even though bile entered the pancreatic ducts. The pancreatic lesion does not occur in dogs when injection is made with a pressure of 800 mm. of bile and seldom with a pressure of 1000 mm. With retching, they say, pressure within the ducts may reach this level. Their experiments do not show that vomiting, which is present at the onset of pancreatic necrosis and may be caused by the passage of a gall-stone, could not force bile into the pancreatic parenchyma.

In 8 cases of hemorrhagic necrosis examined at autopsy by the writer, 5 were associated with cholelithiasis and in 2 of these instances small calculi were found at the orifice of the diverticulum of Vater. In 5 instances described in the literature gall-stones were found impacted at the duodenal orifice of the pancreatic duct. In a similar case described by Thayer the common bile duct was dilated to the size of the little finger and a small calculus was found within the duodenum. In a case described by Pearce no calculi were found but the orifice of the common bile duct was dilated as though a stone had just passed. Among 105 instances of hemorrhagic necrosis collected by Egdahl the coëxistence of cholelithiasis is mentioned in 42 per cent. This figure is doubtless too small to represent the incidence of gall-stones for in many instances calculi have been overlooked or unrecorded.

It is noteworthy that the gall-stones usually found in the bile passages and in the gall-bladder in these cases have been of such small size that they might readily occlude the duodenal orifice of the diverticulum of Vater without closing the communication between the common bile duct and the duct of Wirsung. In only a limited number of individuals is the anatomical structure of the diverticulum of Vater such that a calculus could convert the two ducts into a continuous closed channel. In 1 of 10 individuals examined by the writer the two ducts have no common channel but open separately at the summit of the bile papilla, and in only 32 of 100 normal specimens was the diverticulum of Vater of such size that a small calculus might occlude its orifice without completely

[1] *Arch. of Surg.*, 1923, **6**, 1.

filling it and thus obstructing one or both ducts which enter it. Mann and Giordano[1] claim that only 3.5 per cent. of individuals fulfil this condition but Cameron and Noble found that it was possible in 66 of 100 specimens removed at autopsy to divert fluid from the bile duct into the pancreatic duct by means of a selected gall-stone actually placed within the diverticulum of Vater.

Hemorrhagic Necrosis with Lesions of the Duodenum.—Hlava, who produced hemorrhagic necrosis experimentally with gastric juice, suggested that duodenal contents may be forced into the pancreatic ducts. Polya and Hess produced the lesion by injecting small quantities of duodenal contents into the pancreatic ducts, but Polya and Williams and Busch were not successful when they employed enterokinase alone. Under normal conditions valve-like folds within the orifices of the pancreatic ducts prevent the penetration of duodenal contents.

In a case described by Opie and Meakins hemorrhagic necrosis was limited to the domain of an unusually large accessory duct which entered the duodenum between the pylorus and the orifice of the common bile duct, the pancreatic tissue about the duct of Wirsung being normal. A somewhat similar case is described by Johnstone, and Bassett found hemorrhagic pancreatitis about an accessory duct which terminated at the margin of an inflamed anomalous diverticulum of the duodenum.

Severe inflammation of the duodenum and stomach was associated with hemorrhagic necrosis of the pancreas in 2 cases described by Simon and Stanley who thought that the lesion was due to ascending infection. Duodenal lesions may be secondary to pancreatic necrosis. Hess produced pancreatic necrosis by passing a ligature about the duodenum below the pancreas and inserting a small funnel into the duodenal orifice of the pancreatic duct. He cites cases of Gerhardi and of Konig-Werth in which with acute hemorrhagic pancreatitis there was stenosis of the duodenum below the pancreas.

Hemorrhagic necrosis may be caused by *Ascaris lumbricoides* which have penetrated into the pancreatic ducts. In an instance of this pancreatic lesion accompanied by disseminated fat necrosis Rigby[2] found at autopsy a roundworm projecting from the ampulla of Vater and occupying the lower part of the duct of Wirsung with its end turned into the accessory duct. The common bile duct was dilated and the terminal inch of the duct of Wirsung was stained with bile. In the case of Gallie and Brown[3] pancreatic necrosis with fat necrosis was recognized at operation in a child two and a half years old; fifteen hours after operation a roundworm was expelled from the mouth but its relation to the pancreatic lesion was not more definitely established. It is possible that the worm not only facilitates the penetration of duodenal contents into the pancreatic duct but diverts bile from the bile passages into the pancreas.

Traumatic Necrosis of Pancreas.—Hemorrhagic and gangrenous pancreatitis with disseminated fat necrosis has in a few instances so directly

[1] *Jour. Am. Med. Assn.*, 1924, **82**, 1410.
[2] *Brit. Jour. Surg.*, 1922-1923, **10**, 419.
[3] *Am. Jour. Dis. Child.*, 1924, **27**, 192.

followed abdominal injury that the relation to traumatism cannot be doubted. Injury to the pancreas is usually associated with such severe damage to adjacent structures that a fatal result is rarely referable to the gland. Incisions into the pancreas of animals heal readily, and in 7 of 12 cases cited by Mikulicz-Radecki recovery occurred, although operation had demonstrated a wound of the pancreas. In a small number of cases hemorrhagic and gangrenous lesions have followed blows upon the epigastric region which have not produced superficial wounds. A case is described by Selberg. A man, aged thirty-eight years, was kicked by a horse in the region of the stomach, and was unconscious for a time. There was pain and tenderness in the epigastric region, with gradual distention and vomiting. The temperature remained normal. At autopsy there was generalized fibrinopurulent peritonitis. The omentum was studded with foci of fat necrosis; the head of the pancreas was wholly necrotic, and the remainder of the organ was infiltrated with blood.

Little is known concerning the pathogenesis of traumatic gangrene of the pancreas. Thrombosis of bloodvessels may perhaps explain the lesion. Repeating the experiments of Hildebrand and Dettmer and subsequent observers, Doberauer has shown that obstruction to the circulation, together with other injury to the gland, may be followed by hemorrhagic necrosis of the pancreas and fat necrosis.

Special Pathology.—The appearance of the pancreas varies with the duration of the disease. When death has occurred within forty-eight hours after the onset the organ is much enlarged, and assumes an irregularly cylindrical shape. The areolar tissue in the neighborhood of the gland may be infiltrated with blood and the lesser peritoneal cavity usually contains blood or blood-stained fluid. Opaque white foci of fat necrosis studding the retroperitoneal fat, transverse mesocolon, perhaps the mesentery elsewhere, and the subperitoneal tissue of the abdominal walls, are abundant, particularly in the immediate neighborhood of the gland. The tissue of the pancreas is firm and has in large part assumed a dark red, reddish-brown, or even reddish-black color, and not infrequently presents a mottled or marbled appearance due to the presence of sharply-defined areas of yellowish-white, relatively normal parenchyma. The proportion of transformed parenchyma varies considerably, but rarely, if ever, is the entire parenchyma affected.

Characteristic of the lesion is the widespread necrosis which affects secreting parenchyma, interstitial tissue, and the walls of bloodvessels. Cells are transformed into homogenous structures without nuclei. The architecture of the tissue may be preserved, but outlines of acini and fibrous tissue are often completely lost. Transition from such areas of complete death of tissue to normal parenchyma is abrupt and marked by a zone containing fragments of nuclei, polynuclear leukocytes, red-blood corpuscles, and fibrin. The interstitial tissue of the parenchyma which is still intact is infiltrated with blood, while in the necrotic and partially disintegrated areas occur larger collections of much changed blood. Soon after the onset inflammatory products, particularly leukocytes and fibrin, are found at the margin of the relatively normal tissue.

The pathogenesis of the condition is best studied in the experimental lesion, which does not differ from that which occurs in human cases. Bile and a variety of irritant substances coming in contact with cells of the secreting parenchyma cause their death, and necrosis is associated with such injury to the walls of bloodvessels that red-blood corpuscles escape in great quantity. Hemorrhage may be the result of necrosis before inflammatory changes are well marked, but very quickly evidence of inflammation is found at the margin of relatively intact parenchyma. Flexner and Pearce have shown that degeneration, hemorrhage, and emigration of leukocytes occur within one or two hours after the injection of artificial gastric juice into the pancreatic duct of dogs. There is probably much truth in the suggestion of Klebs that hemorrhage is the result of corrosive action of the pancreatic juice. The various irritant substances which produce the lesion acting injuriously upon the tissue of the organ not improbably subject it to the action of its own secretion.

Gangrene of the Pancreas.—Fitz showed that acute hemorrhagic pancreatitis may terminate in the condition known as gangrene and in at least half of the recorded cases of what he designated gangrenous pancreatitis there was evidence of hemorrhage. In cases of hemorrhagic pancreatitis which have survived a week or more the gland assumes a dark red, reddish-black or black color, and the tissue is dry and covered by changed blood. At the end of the second week the organ may form a soft, black, friable mass, while the lesser omental cavity contains chocolate-colored fluid in which are bluish-black spots. Yellowish spots of softening may occur in the pancreas and the gland may be finally transformed into a soft mass attached by only a few shreds of tissue to the abdominal wall, or, having undergone complete sequestration, according to the description of some observers may lie free in the omental cavity. In such cases the lesser peritoneal cavity is distended with dark bloody or blackish, often foul-smelling, fluid containing particles of necrotic tissue. Infection with a variety of bacteria has occurred, and the abscess cavity thus formed is limited by the lesser peritoneal cavity; the foramen of Winslow is closed by adhesions, and there is in most instances no general peritonitis. The fat about the pancreas and in the wall of the lesser peritoneum is the seat of confluent areas of fat necrosis which as the result of softening and erosion show an irregular surface.

In some instances an extension of the abscess cavity forms a pocket in the retroperitoneal tissue over the left kidney. Perforations, usually with ragged frayed edges, may be found in the wall of the stomach or duodenum, doubtless caused by penetration of the abscess into the viscus.

When, with the experimental lesion, recovery ensues, active proliferation of connective tissue occurs and the newly formed tissue invades and in part or wholly replaces the necrotic parenchyma. Evidences of such reparative changes have been found in patients who have survived the severity of onset, and is doubtless present in the comparatively small number of instances in which complete recovery occurs.

Symptoms.—Fitz carefully defined the symptoms of hemorrhagic and of gangrenous pancreatitis, and although he recognized that many

cases showed varying combinations of the lesions thus designated, described them separately. Most writers who have subsequently described instances of either condition have adopted the classification of Fitz and have used that designation which more accurately describes the anatomical changes which have been found.

Course.—In those cases in which death occurs within a few days after the onset the hemorrhagic character of the lesion is predominant, and those cases which pursue a rapidly fatal course have been described as hemorrhagic pancreatitis. The relation between the duration of the disease and the character of the changes found after death varies considerably, but toward the end of the second week, and in many instances earlier, the pancreas has assumed the appearance described as gangrenous, and those cases have been described as gangrenous pancreatitis in which either the initial symptoms of shock have not been fatal or the onset has been unusually mild. Since the disease apparently pursues a more violent course in men than in women, the hemorrhagic lesion has been more frequently encountered at autopsy in men. When the disease has assumed the subacute course which characterizes most cases of what has been called gangrenous pancreatitis, symptoms due to suppuration and accumulation of exudate in the lesser peritoneal cavity appear.

Stage of Hemorrhagic Necrosis.—Characteristic of the acute disease is its sudden onset, the severity of the pain which is localized in the epigastric region, and the associated symptoms of shock and intense depression of the circulatory system. One group of cases described by Nimier as *foudroyant* terminate fatally within a few hours. Such cases have been described as instances of pancreatic hemorrhage or apoplexy. In a large proportion of instances death occurs within the first four or five days, while about half of the cases pursue a subacute course, death occurring after several weeks or months.

The disease in many instances affects individuals who have suffered with repeated attacks of abdominal pain, but in many cases the patients have had good health, robust men often somewhat corpulent being not infrequently affected. *The preceding attacks of pain* are of two kinds, being referable either to the gastro-intestinal tract or to the bile passages. In nearly one-half of the cases collected by Fitz there had been attacks of indigestion, with pain at times of great severity, nausea, and vomiting. He regarded the previous digestive disturbance as gastric or gastro-duodenal rather than enteric. In about one-fifth of the recorded cases, according to Gessner,[1] there have been, perhaps for several years, typical attacks of gall-stone colic often accompanied by jaundice, until an attack of unusual severity is accompanied by symptoms of collapse.

The *pain of onset*, which appears with surprising suddenness, is of great violence and is localized above the umbilicus; it may be constant or occur in paroxysms, and in the acutely fatal cases persists until death. The pain has been occasionally described as present above the umbilicus and to the left of the median line following the course of the pancreas, but the seat of greatest intensity may be the left or right hypochondrium,

[1] *Deutsche Ztschr. f. Chir.*, 1899, **44**, 65.

or even the lower abdominal region. The epigastric region is sensitive to pressure, and there is usually rigidity of the abdominal muscles. Intense pain in the back radiating toward the legs has been described.

The appearance of pain is rapidly followed by *vomiting*, rarely by nausea alone. Vomiting may recur at short intervals or may stop for several hours or even several days, to be repeated with perhaps equal severity. The vomitus is usually copious and bile-stained, but may be mucous, and in several instances has been dark brown or bloody.

Symptoms of shock accompany the pain and vomiting of onset and usually precede death. There is profound weakness; the pulse is accelerated, and in several instances cyanosis has been a conspicuous symptom. Experiments of Gulecke, Doberauer, and Egdahl[1] indicate that substances perhaps formed by autodigestion of pancreatic tissue depress the circulation and cause profound poisoning.

Although the abdomen is rigid and often distended, particularly in the epigastric region, a *tumor mass* referable to the pancreas is rarely if ever palpable.

In about one-half of the cases there is *constipation*, but in a considerable number of cases diarrhœa is present from the beginning or may follow constipation. The occurrence of constipation in association with the severe symptoms of onset has made the diagnosis of intestinal obstruction in such cases frequent, and the nature of the disease has been determined at operation undertaken to relieve obstruction. Gessner states that passage of feces occurs spontaneously or as the result of enemata in many cases on the fourth day. In 6 cases collected by this author the enlarged head of the pancreas was found either at autopsy or at operation to encroach upon the lumen of the duodenum, but in most cases no anatomical evidence of obstruction has explained the symptoms of intestinal obstruction. It has been suggested that irritation of the solar plexus by hemorrhage or pressure may favor constipation. The stools are not infrequently clay-colored; in 1 case (Chantemesse and Griffon) fatty stools were present, although death occurred two days after the onset of symptoms. The feces rarely contain blood.

Jaundice, varying in intensity, was present in 10 per cent. of the cases collected by Gessner, who has given special attention to the relation between acute pancreatitis and disease of the biliary passages. *Fever* is rarely present during the early stage and with symptoms of collapse the temperature may be subnormal. Elevation of temperature with chill has been observed. *Leukocytosis* has been found in cases in which the blood has been examined. In 1 case the leukocytes numbered 37,000 per cmm. on the first day of the disease. In a case of Sendler their number was not increased. *Diastase* in the feces and urine may be measured by a method introduced by Wohlgemuth; Wynhausen[2] found the enzyme in the feces greatly diminished in 2 cases of hemorrhagic pancreatitis and Hirschberg[3] demonstrated a similar decrease in 2 cases of so-called acute pancreatitis. *Glycosuria* has occurred in only a small

[1] *Jour. Exper. Med.*, 1907, **9**, 385.
[2] *Berliner klin. Wchnschr.*, 1909, **46**, 1406.
[3] *Munchen. med. Wchnschr.*, 1908, **55**, 225.

proportion of cases of hemorrhagic pancreatitis. The case of Benda and Stadelmann is noteworthy, because the symptoms were those of rapidly fatal diabetic coma. The patient became comatose soon after the onset of violent abdominal pain; 3.4 per cent. of sugar was found in the urine. The pancreas, with the exception of a part of the head, formed a soft, bloody mass.

Stage of Gangrene.—Cases in which the early stage has been survived have been described as gangrenous pancreatitis. At the end of several days—Gessner regards the fourth day as critical—the symptoms of onset may diminish in violence; pain and tenderness in the epigastric region are still present, or may recur at intervals, and are not infrequently associated with vomiting. Constipation, if present, disappears and may be followed by diarrhœa. Symptoms which indicate the presence of so-called gangrene, with bacterial invasion of the necrotic gland and adjacent peritoneal surfaces, are fever and epigastric tumor. The transition to the stage of necrosis and suppuration usually occurs toward the end of the second week.

The *temperature*, which during the early stage shows no elevation, is moderately increased and irregular. Although usually little more than 100°, it may reach 104° F., and in some instances there are repeated chills. The disease may, however, pursue its course without fever. *Leukocytosis* was present in two cases of gangrenous pancreatitis described by Thayer. In one case the leukocytes on the nineteenth day numbered 18,300; in the second case during the fourth week they numbered 33,700, although the temperature varied from 97.6° to 98.6° F.

The *tumor mass*, due in great part at least to accumulation of exudate in the lesser peritoneal cavity, usually appears in the epigastric region and, extending toward the spleen, varies considerably in size and distinctness. It has been described at times as a rounded mass the size of a child's head situated above the umbilicus, while in other cases there has been an ill-defined resistance in the same region. In all of 5 cases of gangrenous pancreatitis Körte found a tumor mass which in 3 instances was first found on the left side in the region of the left hypochondrium and flank, subsequently becoming palpable between stomach and colon. In 5 cases described by Thayer a tumor mass was found in the epigastric region; in 2 cases pancreatic gangrene was demonstrated by autopsy, while in 3 recovery followed operation and the nature of the lesion was not clearly defined.

In stout individuals palpation may be difficult, but is facilitated by the emaciation which usually occurs with long continuance of the disease. The muscular spasm which hinders palpation during the acute stage disappears. The lower border of the tumor mass may descend with respiration; occasionally pulsation is transmitted from the aorta, and has been found to disappear in the knee-chest position. Inflation of the stomach and perhaps of the colon may aid in the localization of the mass. Tympany of the stomach separates the mass from the liver, and after inflation of the viscus tends to cover it. The colon lies along the lower border of a tumor mass due to an exudate within the lesser peritoneal cavity. When the abscess cavity eroding the tissue over the

left kidney tends to make its way toward the left lumbar region, resistance may be felt below the left costal margin extending downward as far as the rim of the pelvis.

The stools, which are not infrequently diarrhœal, in a few instances have contained blood. Steatorrhœa has rarely if ever been observed, but in a case of von Noorden's chemical examination showed that the proportion of split fat in the feces was greatly diminished. In 2 cases described by Chiari recovery followed the expulsion from the rectum of necrotic pancreatic tissue.

Jaundice may occur, and was present in one-fifth of the cases of gangrenous pancreatitis collected by Fitz.

Glycosuria is infrequent in pancreatic necrosis. In the cases of Israel and of Fleiner the disease occurred in individuals who had previously suffered from diabetes. In a woman who died with diabetic coma following acute hemorrhagic necrosis Rodriguez[1] found glycosuria and hyperglycemia three days after the onset of acute symptoms. In the case of Brentano 6 per cent. of sugar was found in the urine ten days after operation and four days after the discharge from the wound of a mass of necrotic tissue 12 cm. in length; previous examination of the urine had not been made. Peiser found sugar in the urine two months after the onset of symptoms; it is probable that almost the entire gland was affected, since a few days after the operation a sequestrum of pancreatic tissue 19 cm. in length was discharged from the wound.

Complications and Sequelæ.—The most important complications—namely, cholelithiasis and suppurative peritonitis affecting the lesser peritoneal cavity—have been described. Erosion of the tissue over the left kidney and sinking of the bursal abscess toward the left lumbar region has also been mentioned. Perforation of the stomach, duodenum, and transverse colon occur not infrequently, and in a case described by Thayer the three organs were the seat of erosion. Blood or fetid pus rarely appears in the feces as the result of such accidents. Within the necrotic tissue of the pancreas bloodvessels become the seat of thrombi which not infrequently extend to adjacent vascular trunks. The splenic vein may be occluded and in a case described by Fitz thrombosis of the splenic vein was present in a patient who died ten days after the onset.

Diabetes is infrequently associated with pancreatic gangrene, but may occur either as a complication or a sequel. Such instances have already been cited. In a case of Körte 2 per cent. of sugar was found in the urine twenty months after an operation at which necrotic pancreatic tissue had been removed. Sugar was not present before or immediately after operation; seven years after operation the patient was living but much emaciated as the result of diabetes.

An unusual accident has been described by Langdon. Two years after an operation, at which bloody fluid had been removed from the lesser peritoneal cavity, death occurred suddenly. The pancreas was in large part replaced by scar tissue; the scar was in contact with the portal vein from which fatal hemorrhage had occurred.

[1] *Jour. Am. Med. Assn.*, 1924, **83**, 203.

In a considerable number of cases pancreatic and peripancreatic *cysts* are preceded by acute symptoms which are similar to those of hemorrhagic pancreatitis, but in most instances it is impossible to determine by anatomical examination after a considerable lapse of time the character of the primary pancreatic lesion. A few cases indicate that peripancreatic cysts formed within the bursa omentalis or even pancreatic cysts may follow hemorrhagic pancreatitis. In a case described by Francke intense pain associated with vomiting appeared with great suddenness; two weeks later a tumor was found in the left hypochondriac region and gradually increased in size. At operation, five weeks after onset, an elastic thin-walled cyst, the size of a man's head, occupied the lesser peritoneum and surrounded the pancreas, which was the seat of necrosis and old hemorrhage; foci of fat necrosis were present in the omentum and mesentery. In a similar case of Rasumosky a tumor mass in the epigastrium was noted five hours after the onset of symptoms, and at operation three weeks later was found to be due to a cyst in which necrotic pancreatic tissue was found. Adler[1] has described a so-called pseudocyst of the pancreas which was probably the result of acute hemorrhagic pancreatitis; the pancreas which formed part of the cyst wall was necrotic and the site of old hemorrhage. When blood and necrotic pancreatic tissue remain sterile the digestive ferments of the pancreas may perhaps cause softening and encapsulation by fibrous tissue. The possibility that this process might take place wholly within the substance of the pancreas is suggested by a case of acute hemorrhagic pancreatitis with fat necrosis described by Dressel; a cavity filled with clotted blood the size of a child's head was present within the substance of the gland.

Diagnosis.—For the recognition of hemorrhagic necrosis of the pancreas the mode of onset is important—namely, its suddenness and violence with intense epigastric pain, vomiting, and symptoms of profound collapse. When hemorrhagic necrosis accompanied by constipation resembles intestinal obstruction, the epigastric localization of pain and distention, the intensity of the pain, and collapse point to pancreatic disease. Stercoraceous vomiting is rarely present, and the increase of peristalsis recognizable with intestinal obstruction is not present.

Since the disease may be preceded by repeated attacks of typical biliary colic, and when caused by the lodgment of a small calculus in the diverticulum of Vater is associated with symptoms of gall-stones, a differential diagnosis may be very difficult. When an *attack of biliary colic* is accompanied by pain of unusual intensity, present throughout the epigastric region and perhaps more intense on the left side, especially when there are symptoms of sudden and profound collapse, hemorrhagic pancreatitis should be suspected. With *perforation* of the *gall-bladder* following cholecystitis the symptoms are usually localized on the right side. Ulcerative processes associated perhaps with malignant tumors of the stomach, duodenum, or transverse colon may produce *suppurative inflammation limited to the lesser peritoneal cavity*, particularly when they cause perforation. The suddenness of onset, the intensity of the pain,

[1] *Virchow's Archiv*, 1904, **177**, Suppl. Heft 154.

and the rapidity of collapse indicate the presence of hemorrhagic necrosis of the pancreas, especially when there is no history suggesting gastric or duodenal ulcer or other lesion which might cause perforation of the stomach, duodenum, or transverse colon. Pulsation of a tumor caused by exudate in the lesser peritoneal cavity, being transmitted from the aorta, is not expansile and disappears when the patient rests upon his side or on knees and elbows; Langdon has described such a case simulating *ruptured aneurism.*

When the disease has assumed a subacute course, the recognition of a tumor mass in the epigastric region between stomach and colon suggests the presence of an exudate within the bursa omentalis, but gives positive evidence of pancreatic gangrene only when its appearance follows the acute symptoms already described. Symptoms indicating disturbed pancreatic function such as glycosuria or steatorrhœa are rarely present, but both in the acute and subacute stages chemical methods applied to the examination of urine and feces may give additional information.

Treatment.—Although pancreatic necrosis cannot be directly influenced by any available means, in some instances the profound collapse of onset may be overcome, so that the disease may reach the subacute stage, in which it is more susceptible to successful surgical interference. Intense epigastric pain usually requires morphine, but in several instances the violent pains of onset have been controllable only by inhalation of chloroform. For the vomiting Körte recommends the withholding of food and lavage of the stomach. Enemata may overcome constipation and distention, while nutrient enemata may sustain the strength. For collapse subcutaneous or intravenous infusions of normal salt solution may be employed.

The value of operation during the early stage, when symptoms of circulatory depression are predominant, has been much disputed. Loss of blood is rarely an important feature and it is improbable that hemorrhage from the necrotic tissue could be controlled under the condition which such an operation would present. A mistaken diagnosis, usually of intestinal obstruction, has been the incentive for a majority of the operations undertaken at this stage, and the recognition of characteristic foci of disseminated fat necrosis in the great omentum has given the first indication that the pancreas has been diseased. Careful searching of the intestine drawn out through the abdominal wound, together with prolonged anesthesia, has doubtless had an unfavorable result in many instances. Mikulicz-Radecki recommends evacuation of the hemorrhagic exudate contained in the lesser peritoneal cavity and free drainage of the omental bursa with gauze after exposure of the vault of the diaphragm by resection of the tenth and eleventh ribs, if necessary.

Statistics collected by Gessner indicate that operations undertaken up to the end of the second week and therefore during the stage of hemorrhagic inflammation, are much more frequently fatal than those undertaken at a later period when the disease has become subacute and so-called gangrene with peripancreatic abscess is present. Of 41 instances in which operation was performed upon patients suffering with the disease, 21 occurred during the first two weeks, and in only one case

(Halsted) did recovery follow. In most instances a laparotomy in the middle line was performed, the nature of the disease was not determined, the abdomen was closed, and death followed within a few hours. Of 20 cases operated upon at a later period, when peripancreatic abscess had formed, 6 recovered. In the larger statistics of Mikulicz-Radecki, published about five years later (1903), there were 46 operations in the acute stage, with 9 recoveries, and 35 operations in the subacute stage, with 18 recoveries. This surgeon was unwilling to attribute much significance to these figures, since the relative proportion of untreated cases which die in the first stage is unknown. He maintained that early operation limits the extent of necrosis and sequestrum formation, and gives diminished opportunity for serious complications, such as venous thrombosis and pyemia. Operation under local anesthesia may diminish the tendency to shock. Speese and Klein recommend administration of insulin after operation for hemorrhagic necrosis of the pancreas.

Since the disease is frequently caused by gall-stones, it is desirable to examine the biliary passages at operation, and to determine if calculi are present. The continued presence of a calculus at the duodenal orifice of the diverticulum of Vater may increase the severity of an existing lesion, and its removal is desirable. The calculus which causes the obstruction is usually of small size and not infrequently the gall-bladder has contained a large number of minute calculi, which during expulsion can perhaps repeatedly divert bile into the pancreatic duct. In a patient operated upon ten days after the onset of symptoms Kelly found fat necrosis; he removed from the gall-bladder about fifty very small calculi of almost uniform size; the patient recovered. That the existence of diabetes mellitus should not necessarily prevent operation for pancreatic necrosis is indicated by a case described by Peiser. Before operation the urine contained 4 per cent. of sugar, acetone, and diacetic acid; the glycosuria was not influenced by the evacuation of a peripancreatic abscess. The patient lived five months after operation, and died from diabetes mellitus.

SUPPURATIVE PANCREATITIS

Suppurative inflammation of the pancreas, characterized by accumulation of inflammatory products and softening of tissue, with consequent formation of one or more cavities containing purulent fluid, does not differ from similar changes in other organs. In many instances the disease, which is the result of bacterial invasion, occurs as a primary infection, but in other cases it follows hemorrhagic necrosis of the pancreas, the hemorrhagic and necrotic tissue being particularly susceptible to bacterial infection; hence the so-called gangrenous pancreas may contain abscess cavities, and in such instances a distinction between gangrene and suppuration is impossible. Moreover, acute inflammation of the pancreas, which has persisted for several weeks, almost constantly extends to the lesser peritoneal cavity, which with bacterial invasion becomes the seat of suppurative inflammation. In many cases described as suppurative pancreatitis operation disclosed an abscess in this region, but no

postmortem examination has shown the exact anatomical condition; in reports of many such cases no attempt has been made to distinguish between pancreatic and peripancreatic abscess. With gangreneous pancreatic inflammation, symptoms of peripancreatic abscess may be more conspicuous than those referable to the gland itself, and the lesion at autopsy, several weeks after the onset, may present nothing characteristic of the hemorrhagic and gangrenous lesion.

Etiology.—When suppurative inflammation is not the result of simple extension from an adjacent organ, there are two possible paths of infection—the bloodvessels and the ducts. Metastatic abscesses are rare in the pancreas. Infection by the bloodvessels may explain some cases but more readily demonstrable and probably of far greater frequency is ascending infection by way of the ducts. Experimental studies show that suppurative lesions may follow the injection of bacteria into the pancreatic ducts. Suppurative pancreatitis was produced by Körte and by Carrot by injection of bacilli of the colon group into the duct.

Valve-like folds within the diverticulum of Vater prevent the entrance of the duodenal contents, so that after death it is impossible to force material from the intestine into the duct. The flow of secretion doubtless exerts a protective influence by washing foreign material from the duct. Obstruction of the duct of Wirsung favors the entrance of microörganisms, and many cases of pancreatic suppuration are associated with occlusion of the duct of Wirsung by gall-stones lodged in the diverticulum of Vater, by pancreatic calculi, and by malignant growths compressing the duct. In a case described by Pearce multiple abscesses in the head of the pancreas followed obstruction of the duct by carcinoma of the diverticulum of Vater.

The probability of infection is much increased when the presence of gall-stones has previously caused suppurative inflammation of the bile ducts. In two cases of Mayo Robson's, abscess of the pancreas accompanied cholelithiasis with suppurative cholangitis. In a case of suppurative pancreatitis recorded by Dieckhoff biliary calculi had actually found their way into the duct of Wirsung. In one case it is probable that pancreatic abscess had been secondary to localized hemorrhagic necrosis caused by a gall-stone lodged in the diverticulum of Vater.

In the small number of cases in which bacteriological examination of the purulent fluid has been made, a variety of microörganisms has been found. In the case of Maas and of Etienne both cocci and bacilli were found. In one of the cases described by Fitz several varieties of bacilli and a staphylococcus were isolated. An organism resembling *Bacillus proteus* has been isolated (Hauser); Dieckhoff found diplococci resembling *Diplococcus pneumoniæ* and in a case of Körte streptococci were found.

Pathology.—With acute inflammation of the pancreas there may be polynuclear leukocytes within and about the ducts of the gland, and the interstitial tissue may be distended by œdema. Such inflammation, which doubtless begins as an ascending infection of the ducts, does not necessarily proceed to suppuration, and may be unaccompanied by macroscopic change. It is, however, not improbable that similar infection of greater severity may cause diffuse suppuration in the organ.

In a case described by Etienne[1] the entire gland, which was enlarged, was infiltrated with thick, yellowish, purulent fluid, which collected upon the cut surface; drops of pus escaped from the incised ducts. In other instances destruction of tissue is more advanced and the organ contains communicating cavities of irregular shape filled with pus, or there may be numerous isolated abscesses. In some cases almost total destruction of tissue has been described, a large cavity filled with pus being found to occupy the site of the pancreas. Localized abscesses may be situated in any part of the gland, but are most frequent in the head. The abscess cavity may be surrounded by a fibrous capsule. Fitz observed that fat necrosis occurs less frequently in association with suppurative inflammation than with hemorrhagic or gangrenous pancreatitis; foci of fat necrosis are found when purulent inflammation is the result of hemorrhagic pancreatitis.

Symptoms.—Since suppurative pancreatitis may occur as a complication of acute hemorrhagic pancreatitis, of lithiasis, of cyst, or of cancer, while it is sometimes the result of ascending infection from the inflamed duodenum or bile passages, its mode of onset and symptomatology vary considerably. In one group, including more than one-half of the cases collected by Körte, the onset is sudden and associated with intense epigastric pain, vomiting, and collapse; the symptoms of onset do not differ from those of hemorrhagic necrosis of the pancreas, and it is not improbable that in a considerable proportion of these cases infection and suppurative inflammation have followed hemorrhagic necrosis. The severity of the symptoms diminishes, and the disease in most instances pursues a chronic course, with exacerbations of pain and gastro-intestinal disturbance occurring at irregular intervals. In a smaller group the onset is gradual, and for a considerable time there is abdominal pain, or perhaps only a sense of discomfort in the epigastric region, together with gastric symptoms of variable intensity.

The tendency of suppurative pancreatitis to pursue a chronic course is shown by 14 cases cited by Fitz; 6 were fatal in the first month, 3 during the second month, and 5 between the fourth and eleventh months. In 22 of 46 cases collected by Körte death occurred between one month and one year after the onset. In a few cases death occurs more rapidly.

In most cases there is either *diarrhœa* or *constipation*, the former being present in considerably more than half of the cases. In the case described by Nicholas hemorrhage from the bowel occurred several times, and at autopsy an abscess in the pancreas was found to communicate by a fistulous opening with the duodenum. Hiccough was present in 5 cases collected by Etienne, in 2 of which it was incessant. In 2 of the cases peritonitis may have caused the symptoms. *Jaundice* occurs in a considerable number of cases, and may be due to cholelithiasis, which has afforded conditions favoring infection of the pancreatic ducts. Jaundice may be caused by an abscess situated in the head of the gland and compressing the bile ducts.

Symptoms indicating the occurrence of *suppuration* are fever and

[1] *Arch. de med. exper.*, 1898, **10**, 177.

abdominal tumor. In the greater number of cases there is elevation of temperature, which is moderate in degree, but in some instances the temperature has been normal or even subnormal. In one group of cases, according to Fitz, the onset is violent and there are frequent chills and irregular, often high, temperature, exceeding 105° F.; chills may occur at the onset and recur during the course of the disease. In another group of cases the early symptoms present little that suggests the presence of suppuration; there is loss of appetite, progressive weakness and emaciation, perhaps diarrhœa or jaundice, but no pain or fever. *Leukocytosis* has been present in cases in which purulent fluid has been removed from the lesser peritoneal cavity (Thayer, Murray).

A more or less clearly definable *tumor* mass occupying the position of the pancreas has been noted in hardly more than a fourth of the recorded cases (Körte), but when present this symptom is significant for both diagnosis and operative treatment. In many cases there is abdominal distention not infrequently localized in the epigastric region, and pain and tenderness in the same situation may further prevent satisfactory palpation, which may be more readily performed after the subsidence of the violent symptoms of onset. The detection of deep-seated resistance behind the stomach or between stomach and colon, absent perhaps during the early stage may suggest that the pancreas is the seat of disease.

Disturbances of *pancreatic function*, although significant when present, are not commonly associated with pancreatic abscess, which in most instances leaves relatively normal a considerable part of the gland. Glycosuria has been present in a small number of cases. *Emaciation* associated with suppurative pancreatitis is referred by some writers to functional disturbance of the gland, but is, in part at least, referable to continued suppuration. The accompanying weakness is often extreme.

Sequelæ.—*Peritonitis* due to extension of the inflammatory process to the surface of the organ and subsequent infection of adjacent serous surfaces is almost constantly associated with suppurative pancreatitis. Adhesions binding the posterior wall of the stomach to the pancreas may be the site of fistulous communications with this organ. Encysted peritonitis with effusion limited to the lesser peritoneal cavity is present in cases which pursue a subacute course. General peritonitis has been present in a considerable number of cases examined at autopsy. Rupture of the pancreatic or peripancreatic abscess may occur into a variety of organs. Perforation of the stomach or of the duodenum is not infrequent. Vomiting of purulent fluid and hemorrhage from the bowel have occasionally been associated with perforation of the duodenum. Rupture of an abscess into the general peritoneal cavity has been observed in 4 cases cited by Körte. Thrombosis of the splenic vein extending to the portal vein may occur. In a case described by Bamberger the portal and splenic veins were almost completely occluded by a thrombus which had undergone puriform softening in the neighborhood of an abscess in the head of the pancreas; the liver was enlarged and contained numerous abscesses, the largest of which was the size of a hen's egg. Abscesses in the left lobe of the liver were present in cases of Frison and of Drasche.

Diagnosis.—Since suppurative pancreatitis in a considerable number of instances follows hemorrhagic inflammation, the symptoms of onset are those of the last-named condition, and indeed, even at operation, the distinction between abscess of the pancreas and gangrenous inflammation with peripancreatic abscess is often difficult, although fortunately not of much clinical significance. It is not improbable, however, that pancreatitis which is primarily suppurative may begin with equal severity. In another group of cases the onset is gradual, and there are vague symptoms of gastro-intestinal disturbance with epigastric pain of variable intensity; irregular fever, perhaps with chills, may suggest suppuration. When a deep-seated mass in the region of the pancreas appears, the diagnosis of peripancreatic abscess can be made, but it is rarely if ever possible to decide if peripancreatic abscess accompanies gangrenous inflammation or is the result of an abscess within the substance of the gland. Hence the differential diagnosis between hemorrhagic necrosis and suppurative pancreatitis is rarely possible, since, especially in the early stages the symptoms are those of hemorrhagic necrosis of the pancreas, although the early onset of fever with chills and irregular temperature may suggest primarily suppurative pancreatitis. The symptoms appearing in association with recognizable cyst, lithiasis, or neoplasm of the pancreas, may suggest that suppuration has occurred as a complication of one of these lesions.

When a tumor-like resistance can be felt in the epigastrium behind the stomach and colon, its ill-defined character and its rapid appearance in association with acute symptoms serve to distinguish it from cyst or carcinoma. Nevertheless, the difficulty of diagnosis, especially when the abscess is small, is well illustrated by a case cited by Thayer. An abscess at the junction of the head and body of the gland caused complete obstruction of the common bile duct and presented a picture suggesting carcinoma of the head of the pancreas or of the common bile duct.

Treatment.—Efficient treatment of abscess of the pancreas can be obtained only by surgical methods. Diagnosis is often impossible, but symptoms which indicate the occurrence of suppuration in or about the pancreas suggest the advisability of an exploratory laparotomy, and delay may be followed by grave complications, such as general peritonitis or thrombosis of the portal vein. Nevertheless, the success of surgical treatment is limited by the character of the lesion; with diffuse purulent infiltration and with multiple abscesses of the gland, surgical procedures, according to Körte, will probably be unsuccessful; but when a large accumulation of pus is present within or about the gland, incision of the abscess, removal of its contents, and drainage of the cavity offer opportunity for recovery. Suppuration within the substance of the gland is in most instances rapidly followed by peripancreatic suppuration, but the surgeon who has evacuated pus contained within the bursa omentalis may be unable to examine the gland with thoroughness. In some of the cases upon which operation has been performed an abscess cavity has been limited to the substance of the pancreas.

CHRONIC INTERSTITIAL PANCREATITIS

Chronic inflammation is characterized by increase of interstitial tissue which partially replaces the parenchymatous cells, and is doubtless the most common disease to which the pancreas is subject. It is, however, accompanied by such ill-defined symptoms that it is rarely recognized during life unless an abdominal operation reveals its existence. When the lesion is associated with advanced destruction of the secreting parenchyma, digestive disturbances due to loss of pancreatic juice may result; in some cases the lesion is accompanied by diabetes mellitus.

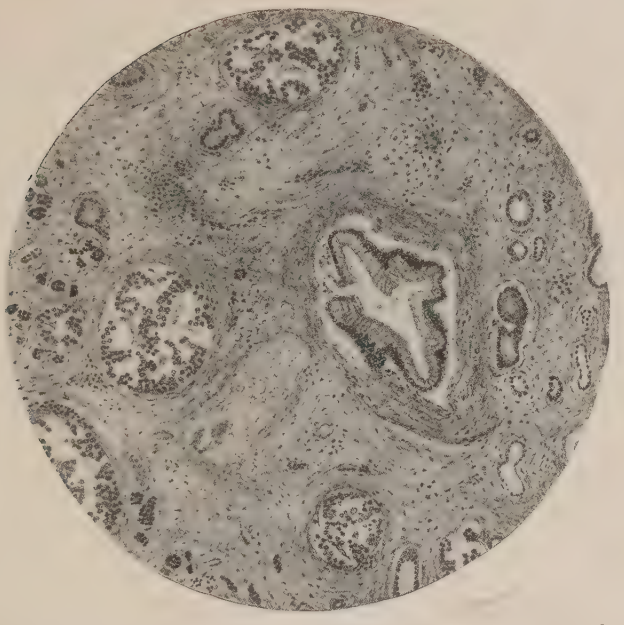
Etiology.—The incidence is illustrated by a series of 30 cases in the Johns Hopkins Hospital, 17 being in males and 13 in females. In five-sixths of the cases death occurred after the fortieth year, while more than two-thirds occurred during the fifth and sixth decades of life. The relation of the disease to gall-stones, carcinoma, and cirrhosis of the liver explains its occurrence during and after middle life.

Partial and complete occlusion of the duct of Wirsung, brought about by pancreatic calculi within it, by large gall-stones lodged in the diverticulum of Vater, or by carcinoma or other new growth, is the most frequent cause. The two ducts of the pancreas anastomose within the gland in nine of ten individuals, and occasionally the duct of Santorini is of large size, being in one of ten cases as large or larger than the duct of Wirsung, but in a much greater number of subjects it is rudimentary in some part; the duodenal orifice especially is often very minute and cannot act as an outlet for the entire pancreatic secretion.

Ligation of the pancreatic ducts in animals is followed by chronic inflammation. The irritant action of the retained secretions and in many cases bacterial invasion of the obstructed duct combine to produce sclerosis, but in human cases the relative importance of the two factors is difficult to determine. Pancreatic calculi, for example, are doubtless in many instances at least produced by an infectious process within the ducts of the gland, and the associated sclerosis may be of such severity that the gland is converted into a fibrous band.

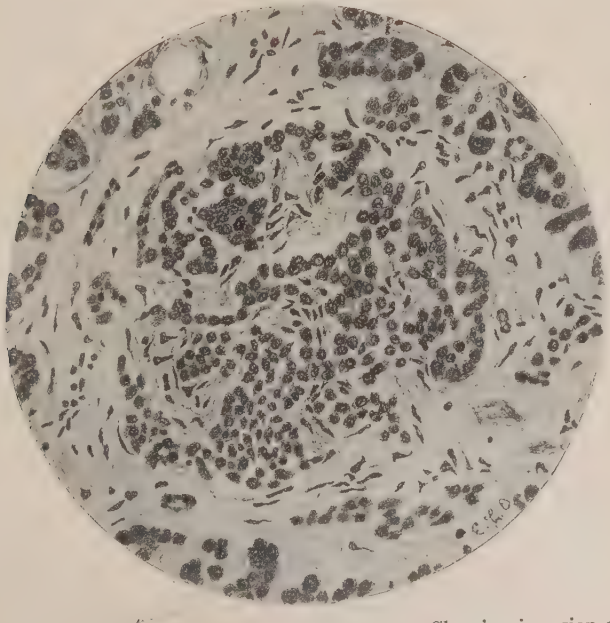
Much attention has been directed to the occurrence of chronic interstitial pancreatitis with cholelithiasis; the consequent induration of the gland when observed at operation undertaken for the removal of gall-stones has not infrequently been mistaken for carcinoma affecting the head of the pancreas. Riedel found in 3 of 122 operations upon the bile passages such dense induration of the head of the gland that malignant growth was suspected; 2 of these patients recovered, while autopsy in a third demonstrated the presence of chronic interstitial pancreatitis. There is little doubt that chronic pancreatitis may follow cholelithiasis, even though no occlusion of the pancreatic duct has been caused by calculi; in such cases acute inflammation of the ducts of the pancreas accompanies similar inflammatory changes in the biliary passages. There is abundant evidence that ascending infection of the pancreatic duct, either from the inflamed bile passages or from the duodenum, may be a cause of chronic pancreatitis. Both Körte and Flexner have caused chronic pancreatitis by injecting colon bacilli and other microörganisms into the pancreatic

FIG. 42



Chronic interstitial pancreatitis following obstruction of pancreatic duct. Showing unchanged islands of Langerhans embedded in sclerotic tissue. (From Journal of Experimental Medicine.)

FIG. 43



Chronic interacinar pancreatitis with diabetes mellitus. Showing invasion of the islands of Langerhans by fibrous tissue. (From Journal of Experimental Medicine.)

duct of animals. In cases of advanced chronic interstitial inflammation examined at autopsy, persistent vomiting accompanied by nausea and epigastric pain afforded evidence during life of gastric or gastro-intestinal disease. It is not improbable that the persistent vomiting produced conditions favoring ascending infection of the pancreatic ducts.

Anastomosis of lymphatics of the pancreas with those of the gall-bladder and duodenum has suggested the possibility that infection may reach the pancreas by these vessels with resulting chronic pancreatitis. Deaver and Pfeiffer have found the lesion limited to the head of the pancreas but since diagnosis has been made at operation by palpation of the gland this evidence has uncertain value. Though transfer of infection by way of lymphatics is possible there is no direct evidence that it occurs.[1] Graham and Petersen[2] produced hepatitis, pericholangitis and inflammation of the pancreas by injecting staphylococci into the portal vein but it is not evident that the pancreatic lesion in these experiments has been secondary to hepatic infection.

Chronic pancreatitis may be referable to changes in the bloodvessels or to toxic substances carried to the gland. *Arteriosclerosis* causes chronic pancreatitis, according to Hoppe-Seyler and Fleiner, and the lesion is analogous to the contracted kidney and to the changes in the liver, heart, and brain following arterial disease. In a case of diabetes with calcification of the posterior tibial artery and gangrene of the foot examined by the writer, chronic pancreatitis accompanied advanced sclerosis of the pancreatic vessels and Hoppe-Seyler described 9 similar cases.

Since alcohol is regarded as one of the most important factors in the production of cirrhosis of the liver, its relation to the similar lesion of the pancreas has much interest. The literature of pancreatic disease contains numerous instances in which the lesion has been found in individuals addicted to the excessive use of alcohol. The lesion in these cases is frequently, although not necessarily, associated with cirrhosis of the liver. Factors other than alcohol producing chronic inflammation act simultaneously upon the liver and pancreas, and chronic pancreatitis and cirrhosis have been found associated by many observers, notably by Kasahara, by Lefas, and by Steinhaus.[3] Among 30 cases of chronic pancreatitis cited above cirrhosis was present in 8.

Pathology.—Interest in chronic pancreatitis has in large part limited itself to the relation of the lesion to diabetes mellitus, and since it may occur with or without diabetes attempts have been made to define the peculiarities of those lesions which cause a disturbance of carbohydrate metabolism. Hansemann described atrophy of the pancreas with diabetes, but in a later paper defined with greater detail the microscopic characters of his so-called granular atrophy and states that it agrees substantially with what has been subsequently called interacinar pancreatitis.

Two types of chronic interstitial pancreatitis are distinguishable. In one type broad bands of newly formed connective tissue occupy the site of the larger trabeculæ of the gland and separate the lobules or groups of

[1] *Jour. Am. Med. Assn.*, 1921, **77**, 194.
[2] *Arch. Surg.*, 1922, **4**, 23.
[3] *Deutsch. Arch. f. klin. Med.*, 1902, **74**, 537.

lobules; areas of surrounded parenchyma are often wholly uninvaded by the sclerotic process; the lesion may be designated chronic *interlobular* pancreatitis. With the second type of chronic inflammation newly formed connective tissue does not form broad bands, but occurs diffusely scattered in small patches and strands, which invade lobules of parenchyma and separate individual acini. The lesion may be called chronic *interacinar* pancreatitis. Among 30 instances of chronic pancreatitis, in 21 the lesion was of the interlobular and in 9 of the interacinar type.

Chronic interlobular pancreatitis results when the duct of the gland is occluded or when the inflammatory process is the result of ascending infection of the ducts. Typical interlobular pancreatitis can be produced in cats by ligation of the ducts of the gland; at the end of a week or more each lobule, which in this animal is unusually sharply defined, is separated from its neighbors by thickened bands of connective tissue. In human cases the most intense grades of pancreatic sclerosis occur with duct obstruction resulting from the presence of pancreatic calculi. The organ may be converted into a narrow band of dense scar-like tissue surrounding the moderately dilated duct filled with numerous concretions. To the naked eye the tissue of the organ altered by interlobular inflammation is firmer than usual, and on section is compact in texture, the areolar character of the interstitial tissue being lost.

At an early stage of the lesion the newly formed tissue shows little tendency to invade the lobules of the parenchyma, and in most instances only their peripheral parts contain invading strands of tissue. At a later stage entire lobules and groups of lobules are completely destroyed, so that a group of several widely separated and atrophied acini embedded in cellular interstitial tissue may be all that remains of one or more lobules. Characteristic both of the experimental and of the human lesion which follows occlusion of the pancreatic ducts is the behavior of the islands of Langerhans. Since the cells forming the islands of Langerhans have no communication with the ducts of the pancreas, they are less affected than the cells of the secreting acini, and often remain wholly uninjured, although the secreting parenchyma has almost completely disappeared. Since intervening acini are replaced by scar-like connective tissue, islands of Langerhans which have been previously separated are brought close together, so that their number may appear to have greatly increased. Embedded in dense, fibrous tissue, the resisting islands of Langerhans finally suffer, possibly as the result of interference with their blood supply. The cells atrophy, and small groups of much atrophied cells scattered in dense stroma may be all that remains of these bodies.

With *chronic interacinar pancreatitis*, characterized by a diffuse new growth of interstitial tissue penetrating between the acini, the organ is tough rather than hard, and does not exhibit the nodular surface seen with the interlobular type. In some instances the organ shows no noteworthy macroscopic change. The newly formed interstitial tissue is somewhat irregular in distribution, so that at one point there may be diffuse thickening of the strands of connective tissue between the acini, while elsewhere occur larger bands or masses of stroma. The interlobular

tissue is not unaffected, but its proliferation is not a constant feature of the lesion, so that the lobulation of the organ is not accentuated, but rather obscured, since irregularly scattered strands of new tissue tend to obscure the interlobular boundaries.

With the interlobular type of inflammation the islands of Langerhans persist, and are affected only when the lesion has reached a very advanced stage; but with the interacinar type, on the contrary, these islands are implicated even when the lesion is little advanced. They are surrounded by fibrous tissue, which forms a capsule separating them from adjacent acini. Within the islands there may be proliferation of interstitial tissue forming coarse strands, which follow the course of the capillaries and separate the columns of epithelial cells. With increase of stroma the cells atrophy or disappear, so that the entire structure is replaced by a minute fibrous scar.

Chronic interlobular pancreatitis, in many instances at least, is referable to an irritant which attacks the glands by way of its ducts. In those instances in which the etiology of the interacinar type is evident, the exciting cause, on the contrary, seems to reach the organ by way of the bloodvessels. Where chronic inflammation is a consequence of arteriosclerosis, it is of the interacinar type; observations of Lefas and of the writer show that many cases of chronic pancreatitis associated with atrophic cirrhosis of the liver, and presumably due to the action of the same cause, which is in many instances alcohol, are interacinar. In some cases the etiology of interacinar pancreatitis is obscure.

Chronic interstitial inflammation of the pancreas, which accompanies *hemochromatosis*, affects the interacinar tissue and implicates the islands of Langerhans; there may be in addition some thickening of the strands of connective tissue between the lobule of the gland. The deposition of an iron-containing pigment in the liver, pancreas, and other glands is accompanied by degeneration of the parenchymatous cells and chronic interstitial inflammation. Bronzing of the skin due to deposition of pigment occurs, and in the later stages of the disease there is diabetes mellitus, the usual cause of death. The pancreas is firm and of a chocolate-brown color due to the presence of yellowish-brown pigment both in the parenchymatous cells and in the interstitial tissue.

Clinical Significance.—Chronic pancreatitis is rarely accompanied by such definite symptoms that its diagnosis is possible, but the relation of disease to other recognizable lesions and its association with diabetes mellitus may suggest its probable existence. Severe pain in the epigastrium and in the mid-scapular region, vomiting, and loss of weight and strength have been noted in association with chronic inflammation of the gland, but are not referable with certainty to this disease which frequently accompanies grave disturbances of the stomach, duodenum, or bile passages. Disturbance of digestion due to loss of pancreatic juice and indicated by fatty stools may occur with chronic pancreatitis, but is usually the result of carcinoma, cysts, or calculi, which occlude the duct and as a consequence cause chronic inflammation.

Pancreatic asthenia as a postoperative complication in patients with

lesions of the pancreas has been described by A. O. Whipple.[1] Profound weakness, continued fall of blood-pressure, anorexia with nausea and vomiting, loss of weight and occasionally ptyalism were found not only after operations for carcinoma of the pancreas but in instances in which the presence of chronic pancreatitis was more or less definitely established. There were, however, associated lesions of great severity and death occurred in one-half of the cases. The relation of the symptoms to chronic pancreatitis is uncertain.

Probable existence of chronic pancreatitis may be suggested by lesions of adjacent organs, particularly when such lesions are accompanied by glycosuria. Chronic interlobular pancreatitis is almost constantly present with carcinoma of the head of the pancreas and with pancreatic calculi, but only when the lesion is advanced and partial destruction of the islands of Langerhans has occurred does diabetes mellitus ensue. Hence glycosuria is present in a relatively small proportion of instances of pancreatic lithiasis and of carcinoma of the gland, Since glycosuria in association with carcinoma, cyst, or calculi indicates far-advanced disease of the pancreas, it has grave prognostic significance.

Riedel and Mayo Robson have emphasized the importance of recognizing at operation chronic interstitial pancreatitis occurring with cholelithiasis. In a certain number of operations for gall-stones the head of the pancreas is so indurated that carcinoma is suspected. In several cases a grave prognosis has been based upon the discovery of induration, but recovery has proved the absence of malignant growth. Mayo Robson believes that chronic pancreatitis should be regarded as a serious complication of gall-stones, at times causing death with increasing weakness and emaciation; cholecystotomy with drainage of the gall-bladder and removal of the calculi, when necessary, is, he maintains, followed by recovery. Induration of the head of the pancreas or of the entire organ in the absence of carcinoma is not definite evidence of the existence of chronic pancreatitis, for the consistence of the gland in the absence of fibrosis varies considerably. Pratt cites instances in which after diagnosis of chronic pancreatitis by the surgeon at operation the pancreas has been found normal at autopsy. Histological examination may fail to confirm a diagnosis of chronic pancreatitis, made by the pathologist because the organ has been found unusually firm at autopsy.

Gall-stones which occlude the pancreatic ducts cause chronic interlobular pancreatitis and associated infection of the biliary passages may hasten the progress of the lesion. Resulting interlobular pancreatitis tends to spare the islands of Langerhans and diabetes occurs only when the lesion is far advanced. Nevertheless, in 36 instances of alimentary glycosuria Eustis[2] found gall-stone disease in 15 and in 6 of these cases symptoms of diabetes subsequently appeared. Joslin believes that gall-stones have a part in the production of diabetes but finds that diabetes with gall-stones is unusually mild.

While chronic interlobular pancreatitis is accompanied by diabetes mellitus in only a small proportion of cases, and occurs only when the

[1] *Ann. Surg.*, 1923, **78**, 176.
[2] *New Orleans Med. and Surg. Jour.*, 1923, **75**, 449.

lesion is far advanced, chronic interacinar pancreatitis which implicates the islands of Langerhans is in almost all cases accompanied by glycosuria. The disease causes relatively slight destruction of the secreting parenchyma and is rarely accompanied by symptoms, other than glycosuria, referable to the gland. In a large proportion of cases it will be impossible to decide during life if diabetes is referable to interacinar pancreatitis. When, however, diabetes mellitus occurs in an individual with cirrhosis of the liver, the former disease is with considerable probability dependent upon chronic interacinar pancreatitis. In cases of diabetes mellitus accompanied by advanced arteriosclerosis, chronic interacinar pancreatitis caused by the arterial disease is probable.

TUBERCULOSIS OF THE PANCREAS

Miliary tuberculosis of the pancreas in association with acute or chronic tuberculosis of other organs is not uncommon, but widespread tuberculosis causing functional disturbance or recognizable enlargement of the gland is almost unknown. Among 128 cases of tuberculosis Kudrewetsky found tubercles in the pancreas in nearly a tenth of them; they were common with acute miliary tuberculosis and with tuberculosis in children. Large tuberculous lesions are uncommon. Chvostek described a case in which the enlarged pancreas formed a fibrous mass containing caseous areas the size of a walnut. In a case described by Sendler a small tumor was felt above the umbilicus in a woman who had suffered with pain and vomiting during nine months; a small mass removed at operation from the head of the pancreas was found to be a tuberculous lymphatic node. Carnot mentioned a case in which the splenic end of the pancreas in contact with a tuberculous kidney was the seat of tuberculosis.

SYPHILIS OF THE PANCREAS

Congenital syphilitic pancreatitis was found by Birch-Hirschfeld in 29 of 124 syphilitic new-born infants. With this lesion increase of the interstitial tissue prevents the development of the secreting parenchyma; the islands of Langerhans resist the process better than the secreting parenchyma, and persist, surrounded by connective tissue. Miliary gummata occur occasionally within the connective tissue which has undergone proliferation.

The pancreas is rarely the seat of gummata occurring with acquired syphilis. Friedreich cited 3 cases in which gummata of the pancreas were associated with characteristic syphilitic lesions of other organs. Cases of pancreatic syphilis in which the lesion is analogous to that of syphilis of the liver have been described by Drozda and by Schlangenhaufer; in association with syphilitic lesions in other parts of the body the pancreas has contained scar-like masses of connective tissue within which are caseous gummata. In a case of Chvostek the tail of the pancreas was penetrated by sclerotic bands which gave it a lobed appearance; gummata

were not present. There are no data with reference to the symptoms or diagnosis of syphilis of the pancreas.

Chronic interstitial pancreatitis accompanying latent syphilis has been described by Warthin[1] who regards syphilis as the most common cause of this pancreatic lesion. Fibrosis occurs, he finds, in patches and is both interlobular and interacinar. He claims that the islands of Langerhans disappear and are replaced by fibrous tissue. In one among 150 instances of what was regarded as syphilitic pancreatitis spirochetes were found. In 6 individuals with syphilis and diabetes changes in the pancreas were the same as those found in other instances of syphilis. In the statistics of the Peter Bent Brigham Hospital, in those of von Noorden and in his own, Joslin[2] found syphilis less common in diabetes than in the general population.

CALCULI OF THE PANCREAS

Pancreatic calculi occur much less frequently than gall-stones. Two instances occurred among 1500 autopsies at the Johns Hopkins Hospital. They occur more frequently in men than in women; among 57 cases collected by Lazarus,[3] 47 were in men and 10 in women. In almost two-thirds of these cases the disease affected individuals between the ages of thirty and fifty years.

Etiology.—The presence of calculi is usually associated with acute and chronic inflammatory changes in the ducts and in the parenchyma of the gland, but etiological relation of these factors to lithiasis is doubtful, since, in part at least, they are caused by occlusion of the ducts or by secondary invasion of bacteria. Guidiceandrea demonstrated the colon bacillus with numerous long bacilli in pancreatic calculi, while in a second case he found in the centre of a calculus numerous cocci and bacilli.

The association of pancreatic and biliary calculi in 8 cases cited by Ancelet and observed by Curnow, Dieckhoff, and Lazarus, suggests that ascending infection from the bile passages, favored perhaps by temporary obstruction of the pancreatic ducts by passing gall-stones, may have caused pancreatic lithiasis, although perhaps both biliary and pancreatic calculi may have been due to the same cause. That stagnation of pancreatic secretion favors the formation of calculi is indicated by cases in which calculi, at times in considerable number, are found within pancreatic cysts. Occasionally an impacted stone has caused the formation of a retention cyst, but in other cases large cysts of obscure origin have contained numerous calculi; Lazarus observed 4 such cases.

Pathology.—In some cases the pancreatic ducts contain fine sand-like concretions, but more frequently several stones, perhaps a centimeter or more in diameter, are present. The largest recorded calculus (Schuppmann) was stellate in shape and measured one and a half inches in its largest diameter. A solitary calculus is rarely found, while several hundred varying greatly in size may be present. In some instances

[1] *Trans. Assn. Am. Phys.*, 1916, **31**, 387.
[2] Joslin, E. P.: *The Treatment of Diabetes*, Lea & Febiger, 1923.
[3] *Beitrage zur Pathologie und Therapie der Pankreaserkrankungen*, Berlin, 1904.

projections from a large stone situated in the large duct extend into adjacent branches, so that a cast of the dilated ducts is produced. In consistence pancreatic concretions vary considerably, being at times mortar-like and friable, but usually hard; they may have a nucleus of organic material consisting of cell detritus. Pancreatic calculi are white, often grayish or yellowish white, but in rare instances black or brownish-black concretions have been found within the ducts.

Biliary calculi have in several cases been found within the duct of Wirsung near its junction with the common bile duct. In an example of suppurative pancreatitis, described by Dieckhoff, the duct of Wirsung was dilated and contained a gall-stone.

Pancreatic calculi are composed in great part of inorganic salts, of which calcium carbonate and calcium phosphate are most abundant, although sodium phosphate, magnesium phosphate, and other salts may be present. Calculi consisting almost wholly of calcium carbonate or calcium phosphate have been described. The composition of calculi from two cases described by Johnston[1] was as follows: (1) Calcium phosphate, 72.3 per cent.; calcium carbonate, 18.9 per cent.; organic matter, 8.8 per cent. (2) Calcium carbonate, 91.65 per cent.; magnesium carbonate, 4.15 per cent.; organic matter, 3 per cent. A calculus with a nucleus of calcium carbonate surrounded by a layer of cholesterin was described by Freyhan. A calculus consisting of calcium oxalate was found at operation in a pancreatic cyst by Shattuck.[2]

Calculi may be situated in the larger ducts or their branches, but calculi of considerable size are usually found in the duct of Wirsung, of which the lumen is frequently so completely occluded that outflow of secretion is prevented and dilatation behind the obstruction results. Stones embedded in ampulla-like diverticula of the large duct have been described. Since the duct of Wirsung is narrower near its duodenal orifice than elsewhere, calculi tend to lodge in this situation, and the duct may be uniformly dilated to a diameter of a centimeter or more. Stones lodged in the terminal part of the duct of Wirsung may compress the common bile duct and cause jaundice; Gould found in the diverticulum of Vater a pancreatic calculus which had caused jaundice.

Obstruction to the outflow of pancreatic juice, doubtless in association with bacterial infection, causes chronic interstitial inflammation of the pancreas, which may reach such an advanced stage that the gland is converted into dense fibrous tissue surrounding the dilated duct, secreting parenchyma having almost completely disappeared. The most intense sclerosis occurs in association with calculi. In the contracting fibrous tissue the islands of Langerhans finally undergo changes, being compressed and invaded by the sclerotic tissue. In cases of diabetes with pancreatic lithiasis the islands of Langerhans have suffered advanced sclerosis (Lazarus, Pearce, Lancereaux, Barron,[3] etc.).

Calculi situated within the ducts not infrequently cause ulceration of the mucosa by pressure. In the immediate neighborhood of a stone

[1] *Am. Jour. Med. Sci.*, 1883, **82**, 404
[2] *Brit. Med. Jour.*, 1896, i, 1034
[3] *Surg., Gynec. and Obst.*, 1920, **31**, 437.

chronic inflammation more intense than elsewhere may produce abundant scar tissue, distorting the duct. The presence of bacteria may result in pancreatic *abscess*, not an infrequent result of pancreatic calculi.

Symptoms.—Pancreatic lithiasis may be unaccompanied by noteworthy local symptoms indicating disease of the organ. Lazarus described such a case in which death occurred with diabetes and pulmonary tuberculosis. At autopsy the pancreas was found to be converted into a fibrous sac and notwithstanding the fact that the duct contained numerous jagged concretions, there had been no pain.

The most frequent symptom is *pain*, which may be continued or intermittent; in some instances there is merely a sense of pressure. More characteristic are attacks of colicky pain, which in some instances have been regarded as sufficiently distinctive for diagnosis. Friedreich doubted the occurrence of *pancreatic colic* analogous to gall-stone colic but severe attacks of colic-like pain occur with the passage of calculi. In a case of Leichtenstern's, symptoms of biliary colic without jaundice were followed by the passage with the feces of three concretions, the largest the size of a pea, composed of calcium carbonate without traces of bile pigments or cholesterin. Pain has been localized in the epigastrium and under the left costal margin in the nipple line, radiating on the left side to the spine or the left shoulder-blade. Pain with pancreatic lithiasis does not necessarily occur to the left of the mid-line, but may be limited to the region of the epigastrium or the umbilicus, or may even radiate to the right side (Eichhorst).

As with biliary colic, the attacks of pain associated with passage of pancreatic calculi are often accompanied by vomiting. Reflex circulatory disturbances, such as weak pulse and temporary collapse, may occur. The pain is at times accompanied by a chill which is followed by fever, possibly referable to bacterial invasion of the occluded duct.

The passage of a pancreatic calculus through the diverticulum of Vater may cause temporary *jaundice*. A patient of Leichtenstern suffered during two years with attacks of a severe abdominal pain accompanied by vomiting and on one occasion by jaundice, but operation demonstrated the absence of gall-stones and autopsy showed numerous pancreatic calculi. The relatively frequent association of cholelithiasis with pancreatic lithiasis may explain the occurrence of jaundice in some instances.

In several instances a diagnosis of pancreatic lithiasis has been made during life from the passage with the feces of calculi composed of calcium carbonate or phosphate and free from bile pigments or other constituents of the bile. In a case of Minnich during twelve days following an attack of colic, soft friable concretions as large as a cherry pip were found, containing carbonate and phosphate of calcium.

Diabetes mellitus, or glycosuria, has been a symptom of pancreatic lithiasis in a large proportion of the recorded cases; Lazarus collected 80 cases, among which glycosuria occurred in 36 (45 per cent.). Pancreatic lithiasis is an infrequent cause of diabetes, occurring only 5 times among 288 cases of diabetes collected from the literature. Pancreatic lithiasis may exist for years without diabetes, and in the case described by Caparelli glycosuria appeared six years after the first attack of colic.

Since glycosuria is not the result of occlusion of the pancreatic ducts but of consequent chronic interlobular inflammation, diabetes results only after the lesion has become far advanced and has injured the islands of Langerhans. At one stage the organ is subject to such slight impairment of function that *alimentary glycosuria* occurs; in the cases of Lichtheim, Lazarus, and Opie, glycosuria disappeared when the patient was given a diet poor in carbohydrates. In the cases of Polyakoff and of Minnich transient glycosuria occurred only after attacks of colic, and was doubtless analogous to that which not infrequently follows experimental injury to the gland, insufficient to cause permanent diabetes. Kinnicutt[1] emphasized the importance of glycosuria as a means of distinguishing the paroxysmal pain of pancreatic colic from that caused by gall-stones.

Steatorrhœa was present in 10 of the cases collected by Lazarus. In the table of Fitz, which contains 29 cases in which visible fatty stools accompanied demonstrable pancreatic disease, pancreatic lithiasis was present in 7 instances. In none of the cases of Fitz was jaundice present, while in 4 there was glycosuria. *Azotorrhœa*, shown by the presence of undigested muscle fibres in the feces, is even less common than fatty stools, and in only 1 (Lichtheim) of the 8 instances in which this accompanied well-authenticated pancreatic disease (Fitz) was the pancreatic lesion caused by calculi.

The *loss of weight* in association with pancreatic lithiasis in the absence of diabetes or disturbances of digestion is probably referable, in part at least, to inflammatory changes or other complications of the disease.

Complications.—Among these the most frequent and serious is *abscess*. Rupture may occur into the peritoneal cavity causing a localized bursal abscess or fatal general peritonitis. A fistulous communication with the intestinal tract may be formed; in a case described by Nicholas and Mollière one liter of blood was passed by rectum two and a half months after an attack of severe epigastric pain; a second attack of colic and subsequent hemorrhage, together with chills, fever, and glycosuria, preceded death. The duct of Wirsung contained about twenty concretions, while in the substance of the gland communicating by a fistulous opening with the duodenum was an abscess from which hemorrhage had occurred. In the case of Caparelli an abscess opened near the umbilicus, and calculi were passed from the fistula which persisted for six years.

The association of cysts with pancreatic calculi has already been mentioned. Cases in which *carcinoma* of the pancreas has been described in association with calculi date from a time when chronic inflammation was not infrequently mistaken for scirrhous carcinoma. In a case of Schupmann carcinoma occupied the tail of the gland, and in the region of the tumor within the duct was a large jagged concretion.

Diagnosis. — Kinnicutt collected from the literature seven cases in which a diagnosis of pancreatic lithiasis was made during life. In the case of Caparelli calculi were discharged from a fistula in the epigastric region, and in the cases of Leichtenstern, Minnich, and Kinnicutt calculi consisting of phosphate or carbonate of calcium without mixture of bile

[1] *Am. Jour. Med. Sci.*, 1902, **124**, 948.

salts were passed with the stools after attacks of epigastric colic. An additional case has been described by Cipriani.

A review of the recorded cases gives no data by which it is possible to distinguish pancreatic from biliary colic, although localization of the pain below the left costal margin may be suggestive of pancreatic lesion. Diabetes mellitus or glycosuria may indicate a lesion of the gland. Fatty stools have been less frequently observed, and in the absence of jaundice have diagnostic value; diminution of split fat in the feces is believed to have similar significance. Jaundice may be caused by a pancreatic calculus lodged in the diverticulum of Vater, or by biliary calculi, which occur with relative frequency in association with pancreatic calculi, and does not exclude pancreatic colic. Simmonds found that pancreatic calculi in specimens removed at autopsy caused distinct shadows in roentgen-ray plates and thinks that radiological methods might aid in their diagnosis.

Treatment.—Statements concerning this are necessarily vague, since few cases have been recognized during life. Attacks of colicky pain have been treated by sedatives applicable to biliary colic. Measures which increase the flow of pancreatic juice have been suggested to overcome obstruction to its outflow, particularly since duct obstruction is believed to be an important factor in the production of calculi. Physiological observations suggest that this may be accomplished by water in abundance, especially when carbonized or acidified by other means; alkalis are thought to diminish pancreatic secretion. To increase the flow of pancreatic juice, Eichhorst injected pilocarpine subcutaneously in a case believed to be pancreatic lithiasis, and the attacks of colic disappeared. It is noteworthy that pilocarpine administered to animals with the pancreatic ducts ligated has caused necrosis of almost the entire abdominal fat, and death within four days.

The presence of glycosuria indicates that the pancreas has undergone grave sclerotic change; nevertheless, in several instances with diabetic diet the sugar has disappeared.

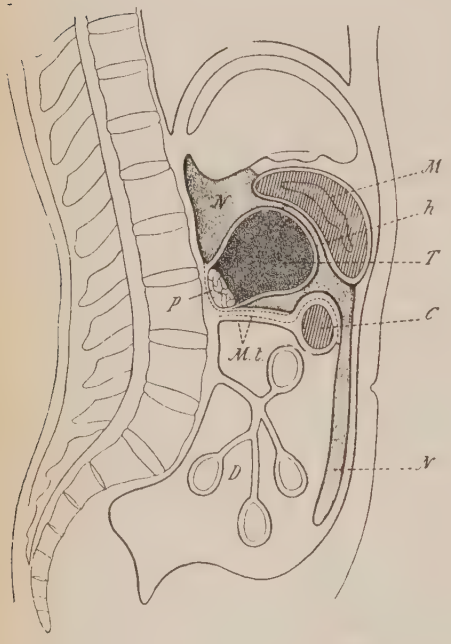
Analogy with gall-stones suggests the possibility of surgical treatment. Gould found at operation upon a patient suffering with symptoms of cholelithiasis a lump at the posterior part of the lesser peritoneal cavity, and on incision removed a calculus from the duct of Wirsung. Obstruction to the flow of bile was not relieved, and at a second operation a stone was removed from the head of the pancreas; although bile subsequently entered the intestine, death occurred as the result of suppuration twelve days later. Moynihan[1] removed through the duodenum a calculus lodged in the duct of Wirsung and projecting into the diverticulum of Vater. Straehlin and Roeber[2] cut into the head of the pancreas and successfully removed several calculi from the duct of Wirsung. Lindsay[3] removed six large stones by incision into the dilated pancreatic duct and recovery followed.

[1] *Lancet*, 1902, ii, 355.
[2] *New York Med. Jour.*, 1905, **82**, 904.
[3] *Lancet*, 1922, ii, 612.

CYST OF THE PANCREAS

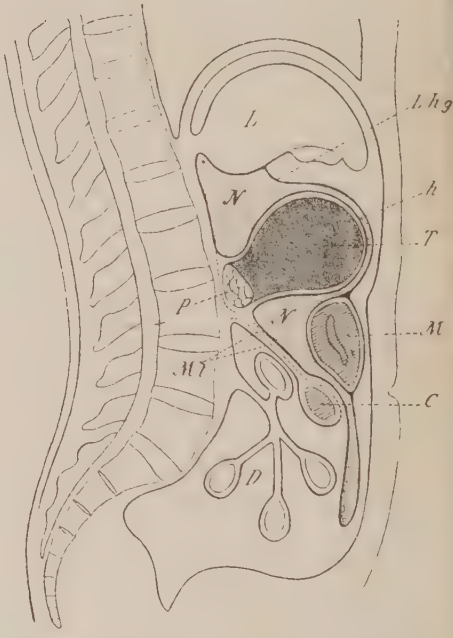
Varieties of lesions are described as cysts of the pancreas; their common character is the presence in the upper part of the abdominal cavity of an encapsulated collection of fluid in contact with the gland and apparently derived wholly or in part from it. Since the greater number of such cysts are observed at operation, the exact nature of the disease is often obscure and its relation to the pancreas is not always established, particularly because fluid encapsulated by the thickened wall of the bursa omentalis may produce signs indistinguishable from those of pancreatic cysts situated within the substance of the gland.

Fig. 44



Cyst projecting into the lesser peritoneal cavity behind the stomach and above the colon. (Oser.)

Fig. 45

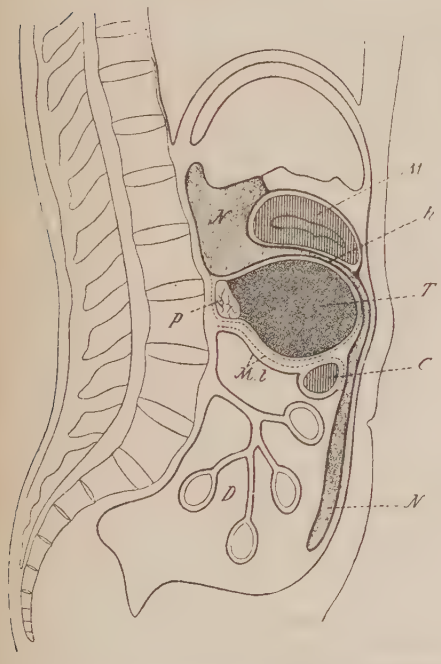


Cyst projecting into the lesser peritoneal cavity, and in contact with the abdominal wall between the stomach and pancreas. (Oser.)

Classification.—True cysts derived from the ducts or acini of the pancreas and lined by a layer of epithelial cells have been distinguished from so-called pseudocysts, which have walls of thickened connective tissue and are without epithelial lining. True cysts may be formed by dilatation of the pancreatic duct or its branches due to obstruction, and are retention cysts, or may be the result of spontaneous proliferation of epithelial structures, and are tumors. Pseudocysts are the result of trauma or of degenerative changes within the substance of the gland, and frequently contain blood or blood mixed with products of pancreatic secretion; pseudocysts may be situated wholly within the substances

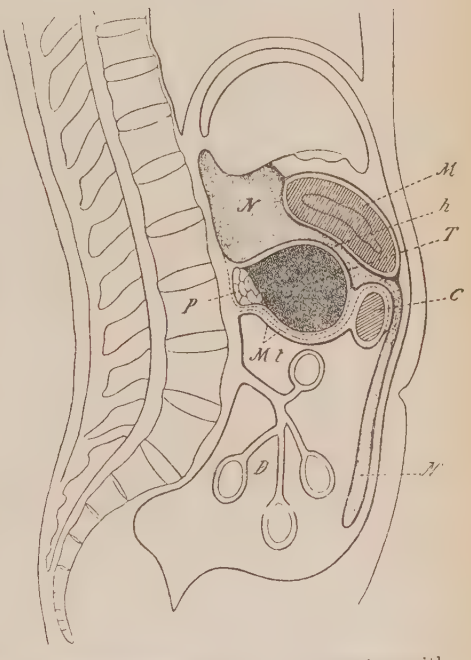
of the pancreas, or, when associated with rupture of the anterior surface of the gland may be limited in part by the walls of the bursa omentalis. Pseudocysts, it has already been shown, may be the result of acute hemorrhagic pancreatitis. The etiology and course of these diverse lesions vary so greatly that it would be desirable to consider them separately were they not characterized by certain physical signs common to all encapsulated collections of fluid having their origin in the pancreas. The relation of different parts of the pancreas to adjacent structures determines the location of such cysts and the point at which they present upon the surface of the body. From an analysis of 133 cysts upon which operation had been performed Körte described the various positions.

FIG. 46



Cyst projecting from the upper surface of the mesocolon and presenting between stomach and colon. (Oser.)

FIG. 47



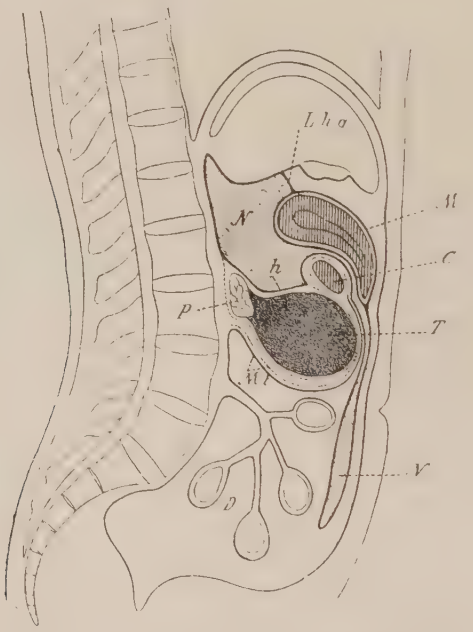
Cyst occupying position of mesocolon, with colon overlying. (Oser.)

A. In the majority the cyst grows directly forward, and, pushing the stomach upward, comes in contact with the anterior abdominal wall between the stomach and colon; in order to reach the tumor at operation it is necessary to cut through the gastrocolic omentum. The cyst occupies and distends the cavity of the bursa omentalis, and, stretching the gastrocolic ligament, may, with increased growth, push downward the transverse colon so that it may reach the symphysis pubis. Pseudocysts which arise from the pancreas and, as the result of rupture of its overlying peritoneum, communicate with the bursa omentalis, and are in large part limited by this cavity, occupy the position described and present

upon the surface of the abdomen between stomach and colon. Jordan Lloyd has shown that accumulations of fluid in the lesser peritoneal cavity due to a variety of causes may closely resemble these cysts of the pancreas. The stomach is compressed and flattened, but usually pushed upward. Should adhesions be formed between the cyst and the stomach, the latter may be held in front of the tumor and drawn downward by it.

B. Less frequently the cyst makes its way above the lesser curvature of the stomach between the stomach and liver, stretching the gastrohepatic omentum which covers it. The upper border of the pancreas is at a higher level than the lesser curvature of the stomach, so that a

Fig. 48



Cyst projecting from lower surface of the mesocolon and presenting below the colon. (Oser.)

cyst arising from this part of the gland may present above the stomach, which, with further growth of the tumor, is pressed downward; with gastroptosis the extent of pancreas above the lesser curvature of the stomach is increased. Körte cites 9 cases in which the cyst presented at operation above the stomach, and in 2 cases described by Riegner and Finotti a diagnosis of the position was made.

C. In a third group the cyst in growing penetrates the layers of the mesocolon. Growth into the mesocolon is more likely to occur when the cyst is situated toward the tail of the gland, since this part of the organ is situated between the layers of the mesocolon; the head of the pancreas being situated in the loop formed by the duodenum, cysts from this part do not find their way into the mesocolon. Körte cites 7 instances

in which the cyst situated in the mesocolon pushed forward the upper layer of the membrane and reached the anterior abdominal wall between the stomach and colon. The transverse colon may be forced downward to the pelvis, and the descending colon may overlie the tumor. In 3 instances the cyst projected upon the under surface of the membrane, so that the transverse colon was found upon its upper margin. Lazarus mentions an intermediate position in which the cyst distends the upper and lower layers of the mesocolon equally so that the transverse colon is found to cross the summit of the tumor.

A case described by Dreyzehner, according to Lazarus, does not belong to any of the groups already defined; this type may be designated prevertebral. A tumor arising from the head of the pancreas forced its way behind the peritoneum to the right of the midline and displaced the right kidney. Payr described a cyst of the pancreas which was found at operation within the larger peritoneal cavity between the liver and pancreas; it had made its way through the foramen of Winslow.

Etiology and Pathology.—Cysts of the pancreas occur with approximately equal frequency in males and in females. About one-half the cases occur between the ages of twenty and forty years. *Congenital cysts* have been described. A cyst the size of an orange (Eha) was discovered in the left hypochondrium of a child five months old; it was attached to the tail of the pancreas and recovery followed removal. Railton found a pancreatic cyst in an infant six months old and Shattuck found a similar cyst in a boy of thirteen months. From the literature Albo[1] collected 24 instances of *hydatid cysts* of the pancreas. Diagnosis in all instances was made at operation or autopsy.

Retention Cysts.—Cysts formed as the result of obstruction of the larger pancreatic ducts or their branches, designated retention cysts, are often of small size and unaccompanied by clinical symptoms. Under the name of *ranula pancreatica* Virchow described dilatation of the duct of Wirsung due to occlusion caused by a villous tumor of the duodenum; the duct had numerous sacculations, giving it a beaded appearance. Klebs described as *acne pancreatica* multiple small cysts containing fluid, sometimes clear and sometimes opaque, yellowish, and thick.

Ligation of the ducts of the pancreas causes only slight dilatation of the occluded channels, and is followed by chronic inflammation of the gland. Complete obstruction to the outflow of secretion in man is usually followed by similar changes. It has been thought that partial or intermittent occlusion may cause cysts. Cysts of the pancreas apparently due to retention of pancreatic secretion have been found associated with obstruction of ducts due to a variety of causes, but the conditions which favor their formation are not understood. Cysts of large size have been found in association with pancreatic calculi. von Recklinghausen found, with a cyst almost the size of a child's head, the duct of Wirsung occluded by a calculus. Lazarus found calculi in the contents of pancreatic cysts in 2 of 14 cases, but suggests that the cyst may afford conditions which favor the formation of concretions. The appearance of pancreatic cysts

[1] *Surg., Gynec. and Obst.*, 1922, **34**, 739.

after cholecystotomy for cholecystitis with gall-stones has been described by Ballini and Saltzstein and by Einhorn.

The walls of pancreatic cysts are usually several millimeters in thickness and are composed of dense fibrous tissue in which remains of pancreatic parenchyma may be found. The inner surface may be smooth and lined by a single layer of cylindrical cells. The presence of such cells indicates the cyst has had its origin in a dilated duct.

Proliferation Cysts.—The occurrence of multilocular cysts of the pancreas, the presence of numerous small cysts in the wall of a large cyst, or the presence of papillary projections upon the inner surface have been regarded as evidence that cysts may be formed by proliferation of epithelial tissue of the gland. In some instances cysts of the pancreas resemble the cystadenomas of the ovary and other organs, and have been regarded as true tumors. Fitz[1] described a multilocular cystoma which apparently had its origin in the pancreas, and collected 9 somewhat similar cases from the literature; 8 cases occurred in women, and in most instances the growth existed for a number of years without causing severe inconvenience. In no case was there evident obstruction of ducts, but a description of some of the cysts does not exclude the possibility that they may have been due to occlusion of small ducts. Körte collected from the literature only 13 instances of proliferation cysts (cystadenomas); Munzer[2] (1903) cites 5 additional cases. In two cases cysts have been associated with malignant growths.

Traumatic Cysts.—Since many cysts of the pancreas contain blood the relation of cyst formation to hemorrhage into the gland has been much discussed, and so-called apoplectic cysts have been described. Hemorrhage may occur into a preformed cyst, and the presence of blood does not indicate that the lesion is the result of hemorrhage. Nevertheless, there is abundant evidence that injuries which cause local hemorrhage may result in the formation of cysts. By crushing the pancreas of a dog Lazarus caused the formation of a hematoma about the size of a pigeon's egg which, after forty days was converted into a cyst with a smooth, fibrous capsule containing 100 cc. of watery fluid. Lazarus thought that the hematoma, together with injured tissue and adjacent parenchyma, had undergone digestion by the secretion of the gland, while a reactive inflammation at the periphery of the lesion had resulted in the formation of a capsule, which prevented the resorption of the fluid contents.

Among 117 cases of pancreatic cyst, Körte found 33 (28 per cent.) in which trauma preceded the appearance of a cyst; Lazarus collected 8 additional cases. In the greater number the epigastric region or the upper left quadrant of the abdomen was the seat of the injury; in several cases there had been compression of the body or a wheel had passed over it. A violent blow or the kick of a horse has preceded the appearance of a cyst. Repeated injury of less severity has been cited as the cause; energetic massage is mentioned by Gussenbauer.

The contents of many cysts which have followed traumatism are bloody, but not infrequently such cysts have contained clear fluid free

[1] *Am. Jour. Med. Sci.*, 1900, **120**, 184.

from blood. The demonstration of one or more ferments either in the contents of the cyst or in the fluid escaping from a fistula after operation has been cited as evidence of connection with the pancreas. Drainage of the cyst has usually been followed by recovery, and in only a few instances have these cysts been studied at autopsy. In the case of Richardson the pancreatic duct communicated with the cyst. Jordan Lloyd maintained that accumulations of fluid in the lesser peritoneal cavity following contusions of the upper abdomen are often mistaken for true cysts of the pancreas. In one case fluid removed at operation had the power of rapidly converting starch into sugar, and was derived in part, he believed, from the injured pancreas.

A number of cases furnish evidence that cysts may follow acute hemorrhagic pancreatitis. The pathogenesis of the lesion doubtless resembles that of traumatic cysts. Hemorrhagic and necrotic tissue undergoes partial solution and subsequent encapsulation by fibrous tissue.

Contents.—These vary greatly, being in many instances mixed with fresh or altered blood. Occasionally clear and watery in appearance, more frequently the fluid is viscid, and in several instances the presence of mucus has been demonstrated. In most instances hemorrhage has occurred into the cyst, and while occasionally the contained fluid may appear to be pure blood, subsequent changes, due in part to the action of digestive ferments, may produce a greenish, brownish, coffee-colored, or even black fluid.

Much significance was formerly attached to the presence of ferments resembling those of the pancreatic secretion, but the absence of one or more of these ferments in the contents of pancreatic cysts and the presence of similar ferments in cysts of other organs has greatly diminished their diagnostic value. The presence of tryptic, diastatic, and emulsifying ferments may suggest the character of fluid removed by operation, but rarely is it possible to demonstrate all three ferments, while most frequently the diastatic ferment alone can be found. The antitryptic action of the blood serum may explain occasionally the absence of trypsin in cysts with hemorrhagic contents. Only when the cyst is in communication with the secreting parenchyma can the ferments of the gland find their way into its contents, while observation on animals (Heidenhain) shows that the secretion of the chronically inflamed pancreas may contain little, if any, ferment.

Fat-splitting, diastatic, or proteolytic ferments, moreover, have been demonstrated in a variety of fluids which do not have their origin in the pancreas. Boas thinks that tryptic ferment is characteristic of these cysts, but Lazarus found a fibrin-digesting ferment in the contents of an ovarian cyst, and it is probable that any fluid containing leukocytes in considerable number will exert proteolytic action in an alkaline medium.

Symptoms.—A rounded *tumor* fluctuating on palpation and situated in the epigastric region behind the stomach and in greater part to the left of the median line suggests a pancreatic cyst, but the variation to which these characters are subject often makes recognition difficult. In the majority of cases the tumor is situated between the ensiform cartilage and the umbilicus, and may produce a rounded protrusion of the abdom-

inal wall. In 48 cases collected by Körte the tumor occupied the median line; in 40 instances the greater part of the mass was to the left of the median line, extending to the left costal margin, and in some instances into the lumbar region. In only 10 cases was the larger part of the cyst to the right of the median line. Very large tumors extend into the lower part of the abdominal cavity, and in 16 cases the tumor extended below the level of the umbilicus, sometimes as far as the symphysis pubis.

The size of the cyst is subject to equal variation; in many instances it is described as the size of a man's head, but may distend the abdominal cavity, extending from the ensiform process to the symphysis pubis. In shape the cyst is usually spherical and the surface is smooth. Fluctuation can usually be felt, but rarely the fluid contents have distended the sac so tensely that the tumor has appeared to be solid. When the cyst is grasped between the hands, pressure of one hand is transmitted to the other. Pancreatic cysts, contrary to the statements of some writers, are not infrequently *movable*, and, particularly when in contact with the diaphragm, move with respiration. Cysts arising from the tail of the gland are particularly movable, and unless fixed by adhesions can be pushed both from above down and laterally. Cysts which lie in front of the aorta may, when sufficiently tense, transmit its pulsation, but cease to pulsate when the patient is in the knee-chest position.

Of much importance is *the relation of the cyst to adjacent organs*, and especially to the stomach and colon, between which in most instances it reaches the abdominal wall. Small cysts may be wholly covered by the stomach, but with increase of their size the organ is pushed upward, so that when artificially distended its tympany separates the dulness of the cyst from that of the liver. The colon, best mapped out after inflation with air, is found along the lower border of the cyst, being in some instances pushed downward to the symphysis pubis. When the cyst occupies the mesocolon, the colon may be below the tumor, may cross its summit, or lie along its upper border in accordance with the previously described relation which the cyst bears to the upper or lower surface of the membrane. When the cyst projects upon the lower surface of the mesocolon, the tumor may occupy the lower part of the abdominal cavity, with its margin in contact with the symphysis pubis. Cysts which force their way between the liver and the stomach produce dulness in contact with that of the liver while their lower part is covered by the stomach, which, when distended, almost completely covers the tumor.

Sudden *disappearance of the tumor* of a pancreatic cyst may be the result of rupture into the peritoneal cavity, In some instances rupture has followed puncture undertaken for diagnosis, or, as in the cases of Halsted and of Schwartz, has followed injury the result of a fall. Of greater interest is the spontaneous disappearance accompanied by temporary diarrhœa of a peculiar character, suggesting that the contents of the cyst have been discharged into the duodenum. Disappearance of the tumor in the cases of Bull and of Karewski was accompanied by the appearance of dark-colored masses in the stools. In the case described by Parson the sudden disappearance of a tumor the size of an orange situated in the epigastrium was followed by profuse whitish diarrhœal

discharge; a second tumor appeared in the lower part of the abdomen at the end of several weeks, disappeared with profuse diarrhœa, and again returned. A large cyst in the epigastrium, described by Payr, disappeared with occurrence of diarrhœal discharges containing whitish particles three times during two months. The conditions which cause the periodic discharge of the cystic contents have not been explained.

Pain is one of the most constant symptoms, and is not infrequently present before a tumor is demonstrable. In a few instances the presence of the tumor has been unaccompanied by pain, or has merely caused a feeling of distention. In a case reported by Marogna a palpable cyst of the tail of the pancreas containing 2 quarts of fluid caused only a slight sense of fulness in the upper abdomen. Pain is usually deeply seated in the epigastric region, or may be referred to the small of the back. In some instances it has been referred to the right or left hypochondrium in accordance with the localization of the cyst in the head or tail of the gland, but little reliance can be placed upon these subjective symptoms. The intensity of the pain varies greatly. It may occur in paroxysms which in some instances have the character of gastric crises, and may be accompanied by vomiting and collapse.

Various symptoms have been produced by the *pressure of the growing cyst upon adjacent organs*. Most constant are those referable to the stomach, which in some instances is flattened by the tumor. Discomfort after eating, loss of appetite, vomiting, and other symptoms of disturbed digestion are present, and may have long preceded other evidence of disease. Compression of the intestine may be accompanied by colicky pain and constipation. In a case of Lazarus the transverse colon situated along the lower margin of the tumor was frequently the seat of colic, and in 4 collected cases complete intestinal obstruction had occurred. A roentgenogram may reveal, as in the case of Einhorn, a pressure defect in the greater curvature of the stomach.

Cysts situated in the head of the pancreas may cause *jaundice*. The relative infrequency of this symptom is explained by the fact that cysts occur more frequently in other parts of the gland. Retention cysts caused by tumors or by biliary calculi compressing the pancreatic duct are accompanied by jaundice due to the same cause.

Compression of the portal vein may be followed by *ascites* and by the establishment of collateral circulation. Dilatation of the mesenteric veins and of vessels upon the surface of the cyst adds to the danger of puncture. Compression of the vena cava has been accompanied by œdema of the lower extremities. In 2 instances (Dreyzehner, Reeve) one ureter has been obstructed.

Functional disturbance of the pancreas has been noted in only a small proportion of the cases, but careful observation of the feces and tests for glycosuria would probably disclose this in a larger proportion. Cysts in the body or tail of the pancreas do not so readily cause such disturbances as the rarer cysts which arise from the head of the gland, since they do not occlude the large duct, and therefore do not cause chronic inflammation of the entire organ. Among 29 instances of *steatorrhœa* accompanying well-authenticated disease of the pancreas (Fitz) this was

referable to cysts in only 2 cases (Bull, Goodman), in both of which diabetes was present as well. In some cases disturbance of protein digestion was indicated by undigested muscle fibres in the feces.

Diabetes mellitus results from the presence of cysts only when the gland is the seat of advanced chronic interstitial inflammation. Diabetes is, however, rarely present. It occurred in only 9 of 134 cases collected by Oser. Alimentary glycosuria in association with pancreatic cyst was observed in a case described by Lazarus.

Loss of weight and weakness commonly accompany pancreatic cysts and may be referred in part to the digestive disturbances and vomiting caused by the pressure of the tumor. Bevan's patient, aged fifty-five years, lost 50 pounds and recovered after drainage of a cyst from which 2 gallons of fluid were removed. One patient developed a cyst in consequence of traumatism and became much emaciated, but after operation recovered so quickly that within six weeks he had regained 15 pounds.

Diagnosis.—Recognition of pancreatic cysts depends almost wholly upon physical signs, although in a comparatively small number of cases diabetes or steatorrhœa confirms the diagnosis. The presence of fluctuation may serve to distinguish cysts from solid tumors of the pancreas or of retroperitoneal structures, but with cysts so tensely distended that this sign is absent some uncertainty may exist, although the spherical shape and smooth surface may indicate the character of the lesion. In determining the origin of such a tumor, of greatest significance is its relation to the stomach and colon, behind which it is situated. This is done best by percussion after inflation. Aid may be obtained by noting the change in position of the stomach during inflation; as the organ enlarges, it gradually overlaps an increasing area at the upper or lower margin of the tumor, in some instances completely covering it. The difficulty is greatest with those unusual cysts which present above the stomach or along the lower margin of the colon, the typical position being between stomach and colon and behind both.

Possible etiological factors may have an important bearing upon diagnosis. A history of injury in the epigastric region may suggest a pancreatic cyst of traumatic origin. Symptoms of hemorrhagic pancreatitis may precede the appearance of a tumor mass.

Since cyst of the pancreas may occupy almost any part of the abdominal cavity, their differential diagnosis presents many difficulties.

Echinococcus cysts of the left lobe of the liver may form large, fluctuating tumors in the epigastric region. The dulness produced by pancreatic cysts occupying their usual position between the stomach and colon is separated by the tympany of the former organ from the area of hepatic dulness, but should the cyst present between liver and stomach, diagnosis is more difficult. The stomach, particularly when distended, is found in front of the pancreatic tumor, which is pushed backward and becomes less palpable, but the organ cannot bear the same relation to a hepatic cyst which lies in contact with the abdominal wall. If a hydatid cyst is punctured, the hooklets or particles of the chitinous layer of the cyst wall may be found. The *distended gall-bladder*, in the usual position of this organ, has the respiratory movement of the liver, and is rarely

covered by the stomach or intestine. Cysts of the head of the pancreas, suggesting a distended gall-bladder, may be accompanied by jaundice.

Cysts of the mesentery have usually been found in the neighborhood of the umbilicus, and, unless fixed by adhesions, are movable in both vertical and horizontal directions. Cysts of the mesocolon are indistinguishable from similarly situated cysts of the pancreas.

The diagnosis between *ovarian cysts* and pancreatic cysts is in most instances made with little difficulty. Pancreatic cysts which arise from the tail of the gland and are situated in the mesocolon lie in contact with the pelvis and may closely simulate ovarian cysts, while cysts of great size distending the abdominal cavity may offer the same difficulty. In some instances the tumor has been first observed in the epigastric region, from which it has subsequently extended downward. With an ovarian cyst examination may demonstrate a pedicle connecting it with the uterus and perhaps dragging the latter upward. With pancreatic cysts the uterus occupies its normal position, and the ovaries are often palpable. Pancreatic cysts of great size are situated behind the stomach and colon, while ovarian cysts push these organs upward.

Pancreatic cysts may closely simulate *hydronephrosis*. The history indicating that the tumor has had its origin in the epigastrium may suggest pancreatic cyst. The tumor of hydronephrosis fills the lumbar region and can be forced even farther backward by distending the colon; pancreatic cysts, as a rule, do not extend beyond the axillary line behind which there is tympany. Periodic disappearance of the tumor may occur both with hydronephrosis and with pancreatic cyst, but abundant flow of urine or simultaneous onset of diarrhœa may suggest one or other condition.

Since pancreatic cysts when tensely distended have been known to transmit pulsations from the aorta, *aortic aneurism* may be suspected. The tumor rises and falls, but has no expansile pulsation; in the knee-chest position pulsation disappears.

Treatment.—Cysts of the pancreas have been treated by puncture, by extirpation, and by incision and drainage. Puncture followed by aspiration has proved ineffectual and dangerous. Kuster and Lazarus mentioned the occurrence of hemorrhage into a cyst due to puncture of enlarged vessels in the wall. When the cyst is infected general peritonitis may follow puncture. Removal of cystic contents by aspiration is usually followed by reaccumulation of fluid, even when the cyst is of traumatic origin and has walls which are not lined by epithelium.

Complete extirpation of a pancreatic cyst was successfully performed in 1882 by Bozemann. The operation is difficult and dangerous, on account of the close proximity of important bloodvessels, and may be followed by diabetes mellitus when a considerable part of the gland is removed. The operation is rarely practicable, unless the cyst has a well-defined wall, and is therefore not applicable to traumatic cysts and other so-called pseudocysts. In several instances complete extirpation has been performed after the multilocular character of the cyst or the presence of papillary projections upon its inner surface has suggested the existence of an adenomatous growth. Complete removal of these

proliferation cysts has been believed to offer the best chance of avoiding recurrence, although in several instances incision and drainage of cysts believed to belong to this type have been followed by recovery. A fatal result is due to gangrene of the intestine, hemorrhage, or peritonitis; when dense adhesions, the proximity of bloodvessels, or the deep situation of the tumor has prevented the completion of attempted extirpation, the mortality has been greater. When a cyst occupies the usual position between stomach and transverse colon, it is in most instances bound by adhesions to adjacent structures, and removal is difficult; when, however, the cyst lies within the mesocolon, adhesions are usually less abundant, and a considerable proportion of cysts which have been extirpated have had this situation. The operation is least difficult when the cyst occupies the tail of the gland, which serves as a pedicle and allows the tumor to be drawn into the wound; it is more difficult the nearer the cyst approaches the duodenum.

When cysts have been partially removed the wound has been drained and healing has occurred by granulation. In most instances of complete extirpation, pancreatic fistula has been avoided, but in two cases cited by Körte pancreatic secretion discharged through the wound. Zweifel removed the entire pancreas save a part of the head 3 cm. in length; glycosuria was present ten days later, and persisted about twelve days, but at the end of two months had disappeared.

The disadvantages of incision and drainage are the occurrence of pancreatic fistula persisting for a considerable period, the possibility of hernia at the site of operation, and the occasional recurrence of the tumor. The resulting wound often heals slowly, and is complicated by the formation of a pancreatic fistula, from which there may be copious secretion. Pancreatic ferments may be demonstrable in the secretion from the wound immediately after operation, or may appear several weeks later; unless care is exercised, there may be erosion of the skin about the wound. The cyst walls collapse, and by formation of granulations the cavity is obliterated. This process cannot be completed when the cyst has an epithelial lining.

A fistula may persist a considerable time; in a case described by Murray a fistula was present during three years. The danger of injecting irritant substances into a fistulous tract is illustrated by a case described by Lazarus; death with collapse, due perhaps to hemorrhagic necrosis of the pancreas, followed the injection of silver nitrate. Infection of a fistulous tract may occur. In some instances there has been hemorrhage from a fistula; curetting of the tract is attended with danger, since dilated bloodvessels may be present in the wall. Closure of a pancreatic fistula has been hastened by making a second posterior opening, thus affording better drainage, or rarely by extirpation of the entire tract.

Healing of a pancreatic cyst is associated with the formation of scar tissue in the pancreas, and chronic inflammation resulting from the presence of the cyst may persist. In some cases in which recovery has followed operation diabetes mellitus has resulted.

CARCINOMA OF THE PANCREAS

Incidence.—In the statistics of Bashford malignant growth was primary in the pancreas in males in 526 among 33,788 instances of cancer, and in females in 474 among 50,000 cases. In the statistics of Segré, among 11,472 autopsies, there was carcinoma of the pancreas in 127 and sarcoma in 2 instances. Among 106 cases of primary cancer collected by Mirallié in 1893, 69 were in men and 37 in women. Cancer of the pancreas usually occurs during middle life, although there have been instances at a very early age. Kuhn described carcinoma of the pancreas in a child two years old, and Simon found the same disease in a boy thirteen years of age.

Secondary Carcinoma.—It is often difficult, when the tumor has attained considerable size, to determine whether it is primary in the pancreas or has invaded it from without. Metastatic tumors occasionally occur in the pancreas, but the organ is more frequently the seat of secondary invasion by cancer of the stomach, biliary passages, or other organs. Since the pyloric region and the posterior wall of the stomach are the most frequently situations of gastric cancer, secondary involvement of the head of the pancreas readily occurs and is followed by chronic interstitial inflammation of the body and tail as the result of compression of the duct of Wirsung.

Pathology.—Carcinoma of the pancreas is much more common in the head than in other parts of the gland. Among 57 cases collected by Segré, the tumor in 19 instances occupied the whole gland, in 35 the head, in 2 the body, and in 1 the tail. In the cases of primary cancer collected by Marallié the head of the pancreas was affected in 82 of 113 cases. Hansemann has described a type of pancreatic cancer which affects diffusely the whole gland. In most cases alveoli of cancer cells are embedded in abundant, dense, fibrous stroma; the tumor is hard and of the scirrhus type. Less frequently the neoplasm is cellular and soft or encephaloid; several cases of colloid carcinoma have been described.

Since the pancreas contains several distinct structures—namely, glandular alveoli, ducts, and islands of Langerhans—the attempt has been made to determine the histogenesis of different types of new growth. In most instances epithelial neoplasms of the pancreas are adenocarcinoma. These tumors, according to Hulst, are probably derived from the ducts of the gland. Where the glandular type is absent and alveoli of the tumor are formed by irregular polygonal cells closely packed together, Hulst[1] thinks it more probable that the tumor has its origin in the secreting alveoli. Nevertheless, in a case carefully studied by Olivier a tumor of the tail of the gland which in part exhibited the last-named type could be traced to the ducts with which alveoli of cancer cells were in places continuous. Fabozzi, from a study of 5 cases of this kind, designated by him *carcinoma solidum*, reaches the conclusion that such tumors are derived from the islands of Langerhans, but Hulst, on the contrary, found no relation between the islands of Langerhans and the alveoli of tumor cells.

[1] *Virchow's Archiv*, 1905, **180**, 228.

Adenoma.—Adenoma, unassociated with cyst formation, occurs rarely, and in most instances found at autopsy has given no discomfort during life. An exception is the encapsulated tumor of the head of the pancreas described as fibro-adenoma by Biondi; it was palpable and caused slight jaundice. Nicholls described a tawny yellow tumor which was the size of a large pea and had the structure of the island of Langerhans; a similar tumor is described by Helmholtz.

Sarcoma.—Sarcoma of the pancreas occurs with far less frequency than carcinoma. Kakels, in 1902, collected 21 instances, among which only 10 were certainly primary in the gland; in 3 of the latter the tumor occupied the tail of the pancreas. Lymphosarcoma, angiosarcoma, fibrosarcoma, and medullary sarcoma have been described. The age of those affected has varied from four to seventy-four years.

Pathology of Complications.—Since *diabetes mellitus* not infrequently occurs with carcinoma, and is due to complete or partial destruction of the organ, the changes in the gland caused by the new growth are of considerable importance. Compression of the duct of Wirsung caused by the tumor mass, which is usually situated in the head of the gland, is followed by chronic interlobular inflammation of that part of the gland from which the outflow of secretion is hindered. The secreting parenchyma is destroyed, while the islands of Langerhans tend to persist in the newly formed fibrous tissue. Pearce has studied the changes caused by the presence of carcinoma. At the edge of the advancing cancer the secreting parenchyma is invaded and replaced by new growth and newly formed connective tissue, but the islands of Langerhans persist in the stroma, and occasionally are uninvaded, even though enclosed by a mass of tumor cells; much hypertrophied islands are found. Carcinoma with permanent glycosuria was present in only one case studied by Pearce, and was associated with advanced chronic inflammation, implicating the islands of Langerhans.

As the tumor increases in size, adhesions may bind it to the stomach, duodenum, and adjacent organs, and symptoms are frequently caused by *pressure of the enlarging mass*. The following possibilities are named by Friedreich, who cites cases in illustration of each. There may be closure of the duodenum or the pylorus, with consequent dilatation of the stomach; occasionally the cardiac end of the stomach is compressed. In one case the stomach was compressed against the anterior abdominal wall. Compression of the transverse colon may cause symptoms of intestinal obstruction. Carcinoma affecting the tail of the pancreas has compressed the left ureter, causing hydronephrosis. Compression of the common bile duct causes jaundice. The growth may compress the superior mesenteric artery and vein, or the splenic artery and vein; pressure upon the portal vein causes ascites, while pressure upon the inferior vena cava causes œdema of the lower extremities. Pulsation of the aorta may be transmitted to the abdominal wall. Necrosis and ulceration may occur in tumor tissue which has invaded adjacent organs, and ulceration of the stomach or of the duodenum may cause the symptoms which are usually associated with primary cancer of these organs.

Symptoms.—When the tumor occupies the head of the gland, *jaundice* is usually present, and, being due to progressive compression of the duct, never recedes, but gradually increases in intensity until finally it merits the designation "black jaundice;" the gall-bladder is distended and is palpable in the usual situation. In 23 of 35 cases of carcinoma of the pancreas described by Heiberg[1] the tumor was limited to the head of the pancreas and in 19 of these cases jaundice was present; in two instances there were no symptoms of pancreatic disease. Cancer of the body or tail of the gland may be unaccompanied by jaundice and other symptoms referable to compression of the biliary passages.

Pain is one of the earliest and most constant symptoms, and is usually seated in the epigastric region radiating toward the back, shoulders, or sternum; the right hypochondrium may be the seat of greatest pain when the tumor is situated in the head of the gland. The character and severity of the pain vary considerably; it may continuously increase in intensity until death, and may be of the intense severity which has been referred by many writers to pressure upon the cœliac ganglion and its branches. Intermittent colicky pain has been regarded as true pancreatic colic due to obstruction to the outflow of the pancreatic secretion caused by compression of the pancreatic duct. Similar pain may be the result of compression of the bile passages.

A *tumor mass* has been palpable in a relatively small proportion of the cases. Mirallié found that the tumor was palpable in from one-fourth to one-fifth of 113 cases which he collected. Futcher found a tumor in 12 of 31 cases verified by operation or autopsy. The tumor must be of considerable size to be felt, especially when the abdominal wall contains abundant fat or is muscular; extreme tenderness may interfere with palpation. Although the tumor is usually immovable, it may descend with inspiration, and occasionally transmits pulsation from the aorta. In some cases the distended gall-bladder has been mistaken for a tumor mass, while at times both tumor and enlarged gall-bladder have been distinguishable.

Symptoms referable to the *gastro-intestinal tract* not infrequently precede more definite evidence of pancreatic carcinoma. There may be lack of appetite or actual distaste for food, especially, it has been thought, for meat, There may be discomfort after eating, eructations, nausea, or vomiting. Compression of the pylorus or of the duodenum may cause dilatation of the stomach, and in some instances symptoms referable to this condition have been the only evidence of the disease (Pilliet). The vomitus in such cases may contain blood. Constipation has been found much more often than diarrhœa, while constipation and diarrhœa may alternate; the stools may be normal.

Disturbance of digestion referable to lack of pancreatic juice in the intestine has been noted more frequently with carcinoma than with other diseases of the gland; but Mirallié found only 9 cases with *fatty stools* among 113 instances of pancreatic carcinoma. Oser collected 8 and Fitz 3 additional cases from the literature. Fitz found only 2 cases

[1] *Ztschr. f. klin. Med.*, 1911, **72**, Heft 5.

in which cancer of the pancreas was accompanied by disturbed digestion of proteins manifested by numerous undigested muscle fibres in the feces. Bulky stools are believed by Oser to be a symptom of pancreatic disease, and occur as the result of imperfect digestion of fats, proteins, and carbyhydrates.

Since carcinoma of the pancreas in a large proportion of the cases invades the head of the gland, *jaundice* due to compression of the common bile duct is frequent, occurring in three-fourths of the cases, and, since the lesion in a large proportion of the cases has its origin in this part of the gland, frequently occurs as one of the earliest symptoms. Carcinoma of the pancreas, next to cholelithiasis, is the most frequent cause of occlusion of the common bile duct, and was the cause of obstruction in 54 of 139 cases of non-calculus occlusion (Ecklin). Jaundice due to compression of the duct may appear suddenly, and, once established, exhibits no remission, but steadily increases. When its sudden appearance is accompanied by colicky pain, cholelithiasis is close simulated.

The condition of the *gall-bladder* and of the liver with obstruction of the common bile duct by cancer of the pancreas has been much discussed. From a study of a considerable number of cases of obstruction of the common bile duct due to a variety of causes, Courvoisier found that with obstruction due to biliary calculi the gall-bladder is usually contracted, while with occlusion due to other causes the gall-bladder is usually dilated. The statistics collected by Ecklin confirm this view. Among 172 instances of obstruction of the common bile duct due to gall-stones, the gall-bladder was contracted in 110, normal in 34, and dilated in 28 cases. On the other hand, among 139 instances in which the common bile duct was obstructed by other causes, the gall-bladder was contracted in only 9, normal in 9, and dilated in 121 cases; among 62 of these cases constriction of the common bile duct was due to carcinoma of the pancreas, and the gall-bladder was dilated in 58 instances. Contraction of the gall-bladder with biliary calculi is the result of inflammatory changes, whereas, with obstruction due to carcinoma of the pancreas or other cause, inflammation is usually absent and the gall-bladder is dilated.

Bard and Pic attached much importance to absence of enlargement of the *liver* with carcinoma of the pancreas. Mirallié, nevertheless, found the liver enlarged in 17 cases. In the cases of Friedreich and of Kellermann the liver contained, during the terminal stage of the disease, secondary nodules of large size.

Compression of the portal vein may cause *ascites* and other evidences of portal obstruction, such as swelling of the spleen and hemorrhoids. In 13 of 113 cases of primary carcinoma collected by Mirallié, ascites was present. Cases with chylous ascites have been described.

Glycosuria and other symptoms of *diabetes mellitus* not infrequently accompany cancer of the pancreas; among 50 cases Mirallié found glycosuria in 13, and Oser collected 10 additional instances of glycosuria. Diabetes was present in 2 cases described by Pearce, and alimentary glycosuria in 1. Cancer of the pancreas is an infrequent cause of diabetes. The glycosuria of pancreatic cancer may disappear before death.

Cachexia is said to proceed with special rapidity when the pancreas is the seat of the disease. Partial exclusion of pancreatic juice from the intestine and obstruction to the outflow of bile doubtless contribute to cause weakness and emaciation. Kellermann, who described a case of cancer of the pancreas without cachexia, found only 3 similar cases.

The *temperature* with carcinoma of the pancreas is normal or subnormal unless there are complications accompanied by infection.

The *duration of the disease* after onset of symptoms is short; in 13 instances cited by Herringham 2 lived seven months, 3 for six months, 6 from four to six months and 2 less than four months. Speed[1] found the duration of symptoms in many instances only a few months.

Diagnosis.—The features of greatest importance are jaundice increasing gradually, attaining great intensity, and associated with dilatation of the gall-bladder, the presence of a tumor in the epigastric region, rapid emaciation, and advanced age. In the absence of both tumor and jaundice diagnosis is hardly possible. Symptoms indicative of impaired pancreatic function are present in a relatively small proportion, but give definite evidence that the disease is located in the gland.

When jaundice is present, differential diagnosis between *cholelithiasis* and carcinoma is important. In certain cases of pancreatic carcinoma biliary symptoms serve to distinguish the two lesions. Jaundice usually appears gradually with carcinoma and increases without remissions, while with biliary colic the onset is more sudden and the progress more interrupted. Impacted calculi may, however, cause progressively increasing jaundice of great intensity; the gall-bladder is dilated in only a sixth of the cases, but with carcinoma of the pancreas, on the contrary, the gall-bladder is dilated with few exceptions. A palpably enlarged gall-bladder, therefore, gives evidence that cholelithiasis is not present, but the absence of this symptom is not equally significant, since the dilated organ is not always palpable, particularly when the abdominal wall is thick. Rapid emaciation and intense epigastric pain point to cancer of the pancreas. With carcinoma the temperature is usually normal or subnormal, but with cholelithiasis fever is not infrequent.

Jaundice caused by *carcinoma of the liver, bile passages, duodenum, or stomach, compressing the common bile duct*, has a gradual onset and progressive character, but emaciation and weakness are said to occur less rapidly than with carcinoma of the pancreas. Tumor has been recognized in a relatively small proportion of cases of cancer of the pancreas, but doubtless this proportion would be much increased by examination under anesthesia with the stomach and colon empty. A tumor mass having its origin in the head of the pancreas is deeply situated in the epigastric or umbilical region, and is usually defined with difficulty. The tumor is usually less movable than tumors of the pylorus or of the colon, and its position is unaffected by distention of these organs. Radiological evidence of increase in the size of the duodenal curve may be obtained in some instances with tumor of the head of the pancreas and Buckstein[2] has devised a method by which the duodenum may be completely filled with barium. Pulsation transmitted from the aorta is not expansile. Both dilatation of the stomach and intestinal obstruction

[1] *Am. Jour. Med. Sci.*, 1920, **160**, 1.

[2] *Surg., Gynec. and Obst.*, 1924, **39**, 509.

may be caused by carcinoma of the pancreas. The diagnosis between primary carcinoma of the pancreas and malignant growth arising from the common bile duct or duodenum is scarcely possible.

Tumor mass due to *carcinoma of the tail of the pancreas* may be mistaken for cancer of the cardia or of the colon. Takayasu described a case in which an apparently immovable tumor, the size of a hen's egg, was felt behind the left rectus muscle. With inflation of the stomach, which lay above it, the tumor partially disappeared, and with inflation of the colon, which was at its lower margin, disappeared completely. Operation confirmed the diagnosis of carcinoma of the pancreas. A defect in the mid-part of the greater curvature of the stomach shown by roentgenological examination is usually caused by neoplasm of the stomach wall but with other evidence of pancreatic disease should suggest carcinoma of the tail of the pancreas.

Treatment.—Medical treatment is directed to alleviation of pain, jaundice, digestive disturbances, and diabetes. The administration of an emulsion prepared from the fresh pancreas of a pig has been found to aid digestion of fats and protein when obstruction of the ducts prevents entrance of pancreatic juice into the intestine (Fles); for the same purpose commercial pancreatin has been recommended.

In a small number of cases tumors of the pancreas have been removed by *operation*. In a considerable proportion of the cases the patient has survived the immediate effects of the operation. Of 17 instances of resection of the pancreas for tumor collected by Finney (carcinoma, 10; adenofibroma, 2; sarcoma, 4; doubtful, 1) recovery occurred in 8. All deaths were associated with extensive malignant tumors with adhesions. In 3 instances, including Finney's case, the pancreas was completely divided and the cut ends were brought together by sutures; recovery followed in all of these cases. It is noteworthy that among the tumors which have been removed those types which are least frequent among pancreatic tumors have been relatively common; in 4 cases the growth arose from the tail of the gland, causing a palpable tumor on the left side of the abdomen. Billroth and Franke believed that they had removed the entire pancreas, but this was not confirmed by autopsy; in Franke's case sugar was found in the urine from the fifth to the nineteenth day after operation, and death occurred in five months.

For the *relief of complications* a variety of palliative operations have been performed, but it is doubtful that they have materially prolonged life or added to the comfort of the patient. When jaundice due to compression of the common bile duct has caused much discomfort, cholecystenterostomy has been performed. In several instances the patient has lived from six to eighteen months, and the condition apparently has been improved. Little improvement has followed the formation of an external biliary fistula, and death has usually occurred a short time after operation (Nimier). When persistent vomiting and dilatation of the stomach indicate compression of the pylorus or duodenum, gastro-enterostomy may give relief, but since the biliary and pancreatic ducts are usually compressed, the operation in pancreatic carcinoma has not the advantages which it offers for the relief of the symptoms of pyloric carcinoma.

CHAPTER XIII

DISEASES OF THE LIVER, GALL-BLADDER, AND BILIARY DUCTS

By the Late A. O. J. KELLY, M.D.

REVISED BY

B. B. VINCENT LYON, M.D.

THE LIVER[1]

DISORDERS OF FUNCTION

The liver, the largest glandular organ in the body, is of complex structure and is endowed with a multiplicity of functions. Several of the structural peculiarities are mentioned in the discussion of the histology of cirrhosis, and the structural changes in different diseases are discussed under the respective headings. The disorders of the functions are less understood. In some instances the structural alterations cannot be detected but their existence can hardly be denied, and we must regard the symptoms—the presumptive evidences of disease—as manifestations of structural alterations. Usually noteworthy symptoms are associated with more or less demonstrable structural alterations; but extreme disorder of function is not infrequently associated with apparently normal structure, and even advanced structural alterations are not incompatible with long life and freedom from distress. It is essential to correlate function with structure, and to study diseased processes from the structural, the functional, and the chemical points of view.

The functions of the liver may be said to be: (1) To secrete bile; (2) to maintain the blood-sugar level (Mann) by storing glycogen derived from the carbohydrates, or from the non-nitrogenous part of the proteins when the supply of carbohydrates is deficient, converting the glycogen into glucose and liberating it when required; (3) to assist in the metabolism of the proteins to the extent, at least, of forming urea from ammonia compounds, or destroying uric acid; (4) detoxifying poisons that enter the body by way of, or are elaborated within, the gastro-intestinal tract or are perhaps produced elsewhere; (5) to destroy or render inert such bacteria as enter the body by way of or are elaborated within the gastro-intestinal tract; (6) to warehouse some of the fat taken as food and to release it when the supply from without becomes deficient; and (7) the liver plays a role in iron metabolism, as yet little known.

[1] The best work on the subject is Rolleston's *Diseases of the Liver, Gall-bladder, and Bile Ducts*, a record of much personal observation, including a thorough review of the literature with many statistics and selected case-reports in brief.

Disorder of the functions of the liver may be primary or secondary (to structural alterations in the liver or to disease elsewhere); and it may be partial, involving perhaps only one function, or it may be total, involving presumably all the functions. The belief in a primary general disorder of function is exemplified in the terms "torpid liver," "biliousness," "bilious headache," etc. Present-day opinions tend, perhaps unwisely, to minimize the influence of the liver in these disorders; but this seems an almost inevitable result of the knowledge that phenomena commonly attributed to a supposed torpid liver may result from factors that do not involve the liver primarily, if at all. The dyspeptic symptoms of a supposed torpid liver are usually due to gastro-intestinal catarrh set up by dietetic indiscretions, excessive eating (especially of proteins and carbohydrates), excessive use of alcohol, focal intestinal infections, etc. The spread of this catarrh to the diverticulum of Vater and the common bile duct, or perhaps a descending cholangitis, accounts for the subicteric tint of the conjunctiva and skin in some patients.

There is, however, another series of cases, such as the passive congestion of chronic cardiac disease, in which there is reason to believe that the functional activity of the liver is reduced. It is usually difficult, if not impossible, in these cases to differentiate the symptoms referable to disordered functions of the liver from those due to the defective circulation in general with consequent congestion of different organs, notably the intestines and kidneys, and defective elimination. It is not unlikely, however, that the headache and other nervous symptoms, digestive disturbances, and loss of flesh and strength that occur in these cases are due, in part at least, to the disordered functions of the liver. This is perhaps due directly to the influence of enterogenic poisons which, being carried to the liver by the portal circulation encounter an organ reduced in vitality by the long-continued passive congestion, and incapable of exerting its detoxifying function; the toxins, in consequence, pass over into the general circulation and cause at least some of the symptoms.

In another series of cases, more or less complete functional failure of the liver ensues. These are cases of severe intoxication or infection, in which widespread destruction or disorganization of the hepatic parenchyma occurs. The striking clinical phenomena, which may develop suddenly although they are sometimes preceded by minor symptoms, are for the most part nervous; they are variously designated hepatargia, acholia, cholemia, hepatic auto-intoxication, etc. Headache is a conspicuous symptom and is soon followed by mental excitement, delirium (even active or maniacal), muscular twitchings, and convulsions; or mental hebetude progressing to deep coma may ensue. Most of these cases are associated with varying grades of jaundice and other phenomena more fully discussed later.

I. The Bile Secreting Function.—It is generally agreed that the polygonal cells of the liver manufacture the fluid called bile. This fluid must be considered an excretory fluid, as well as secretory, since, by means of it, various components of the bile presumed, if not actually known, to be of a toxic nature leave the body by way of the intestinal canal. Surprisingly little accurate information is available as to the exact chemical

and physical properties of human bile in health and disease. Most work heretofore has been done on gall-bladder and duct bile obtained at or after operation or on bile from the gall-bladder obtained at necropsy. More recently, by non-surgical drainage of the biliary system, large amounts of human bile are obtainable for study and new data have been furnished. Practical clinical methods for investigating the chemical constituents of such biles have not been developed, although a beginning has been made by McClure and his co-workers.[1] Obvious difficulties exist because the fluids obtained by duodenal intubation represent mixtures secreted by the salivary glands, stomach, pancreas and duodenum, as well as the bile secreted by the liver, and the chemical nature of this mixture cannot readily or accurately be proportioned or dissociated. Among conflicting theories and opinions this may be conservatively stated. The *bile salts* appear to be derived from the parenchymatous cells of the liver alone and in addition to being excreted in the bile are reabsorbed in the intestines and carried back to the liver by the portal blood. The bile salts (especially taurocholic acid) appear to be the most potent agent in stimulating bile secretion and bile discharge. Much experimental discrepancy exists regarding the cholagogic action of the salicylates, epinephrine, pilocarpine, atropine, dilute acids, glycerin, calomel, etc. The view that pro-secretin manufactured by the duodenal cells, when activated into secretin by the hydrochloric acid of the stomach, acts as a stimulus to both liver and pancreas still remains unchallenged. Foods vary materially in their ability to encourage or retard bile flow. A meat diet favors an abundant flow of bile in fistula dogs whereas a high carbohydrate diet—especially sugar—slows the flow (Whipple). Vitamine in brewer's yeast is said to stimulate bile flow but this has not been experimentally checked. Several investigators (Oertel, Blankenhorn) believe that in mechanical obstruction of the liver ducts the secretion of bile may be retarded from intrahepatic pressure. Observations on biliary fistula, as well as clinical observations, indicate that nervous influences, nervous shock, etc., can vary (usually slow) the rate of bile discharge. This phenomenon is repeatedly observed during duodeno-biliary drainage. It is especially common in the neurolabile races as seen in America, particularly Hebrews and Latin-Americans.

As to the *bile pigments*, the view that the liver is necessary to their manufacture must now be abandoned. Mann[2] has proved that the liver is not essential for the formation of bilirubin and that probably a high percentage of the bile pigment normally excreted by the liver is manufactured elsewhere. Its most likely source is from the "reticulo-endothelial system." The Kupffer cells of the liver participate in bile pigment metabolism but are not alone essential to its formation. Conclusions drawn from Rich's work[3] support this view. Mann's experiments have also shown that, due to the extrahepatic formation of bilirubin, a true hematogenous jaundice can and does occur after total removal of the

[1] McClure and Vance: *Boston Med. and Surg. Jour.*, 1924. McClure, C. W., Mendenhall, W. L., Huntsinger, M. E.: *Jour. Am. Med. Assn.*, 1925, **85**, 1537.

[2] *Am. Jour. Physiol.*, 1924, vol. **69**.

[3] *Johns Hopkins Hosp. Bull.*, 1923, **34**, 321.

liver. Bloodvessel endothelium (including Kupffer's liver cells) and mesothelium of the serous cavities can rapidly change hemoglobin into bile pigment. Van den Bergh's work on detection of bile pigment in human serum has been of great importance and suggests that there are at least two forms of bilirubin, a free pigment and one partially bound. Whipple has worked out a conception centreing around his "pigment complex" which he believes represents an intermediary stage in the development of mature pigments and thinks that all pigment units pass through this stage, and are used to construct hemoglobin or bile pigment, or are discharged from the body as urobilin, urochrome or related pigments, depending upon supply and demand. He believes that stercobilin is not absorbed from the intestines and that urobilin as observed in the urine, is formed in the liver or body tissues and not absorbed from the intestine. He believes the bile pigments are true excretory products of the liver which serve no useful purpose. They do not take part in the "circulation of the bile" which is limited to the bile salts. More recent experimental work[1] suggests the possibility of an entero-hepatic circulation of bile pigment and that both bilirubin and urobilin are capable of absorption from the intestinal tract.

Other Components of Bile.—The bile also holds in solution various other substances, among which are cholesterol, calcium, lecithin, leucin, tyrosin, etc., which are excreted by the liver when in excess and are thus concerned with general metabolism. Some of them, notably cholesterin and calcium, are in part at least, furnished by the food. When an over supply is provided the liver bile appears unable to hold them in solution and the excess is excreted in a crystalline form readily recognizable in microscopic preparations from human bile obtained by biliary drainage. The attempts of McClure to devise quantitative colorimetric methods of estimating the amount of such substances in the bile are promising, notwithstanding the "variables" due to the intermixture of other tissue secretions. An important point to be explained is whether such crystalline and fatty substances when thrown out of solution in the liver bile are due merely to oversaturation or to a defective function of the liver cells by which they are unable to secrete bile capable of holding in solution the normal amounts. This would throw additional light on the mechanism of formation of gall-stones. The fact that clinical improvement and disappearance of abnormal findings with parallel improvement in abnormal blood chemistry have followed non-surgical drainage may indicate that the damaged liver cells are recovering or that the remaining healthy cells are being stimulated to function more actively.

The Amount of Bile Secretion.—Heretofore it has been generally considered that the liver secretes from 1000 to 1500 cc. of bile in twenty-four hours, based largely on the amount recoverable by surgical drainage of the gall-bladder or major bile ducts. By the continuous method of non-surgical drainage it is possible to recover much larger amounts in twenty-four hours—up to 4000 cc. of a bile mixture representing salivary, gastric, duodenal, pancreatic, and biliary fluids; by far the largest amount is bile.

[1] Broun, McMaster, Rous: *Jour. Exper. Med.*, 1923, **37**, 699; McMaster and Elman: *Jour. Exper. Med.*, 1925, **41**, 513 and 719.

In some instances this seems to represent the total bile output, since the stools have become acholic, whereas in other cases the bile output is even larger since the stools contain bile. Conclusions drawn from such observations are that the liver probably has a secretion capacity considerably greater than 1500 cc. in twenty-four hours. Another point is the large amount of bile (often 1000 cc. of the mixture) recovered during the overnight drainage period, in the so-called interdigestive or rest period, when Oddi's sphincter is generally considered to be in a state of tonus and bile therefore is being stored in the ducts and gall-bladder. This may be in favor of dysfunction of Oddi's sphincter.

Whipple and others have noted that a bile-fistula dog often excretes considerable amounts of bile during fasting periods but in such experiments Oddi's sphincter control is interfered with. A further disturbance may be evident; normally, both bile pigment and bile salts, after passing into the bile capillaries, may be absorbed into the general circulation in cases of complete obstructive jaundice where there is gross obstruction of the ducts. In many cases such obstruction, even in the small bile ducts, cannot be demonstrated and in such cases there is often dissociated jaundice, the bile pigment passing into the circulation and the bile salts passing into the intestine. Van den Bergh's test differentiates these types. By Brulé and Lemiere's blood test, it can be shown that the digestion of fat due to the presence of bile salts in the intestines still continues; if the blood one and a half hours after eating shows the presence of hemoconia (minute particles of fat) then fat is being absorbed, whereas in complete obstructive jaundice hemoconia are not found in the blood because of the absence of bile salts in the intestine. If the hepatic cells fail in secreting sodium cholalate (the normal solvent of cholesterin) precipitation of cholesterin crystals will occur in the bile. The newer work, particularly of the French school, definitely claims the existence of dissociated jaundice and supports the belief that one form of jaundice may be due to a functional defect in the liver cell whereby bile pigment may be passed into the circulation instead of into the minute bile ducts. This functional disturbance produced by some poisons, can be shown to follow the injection of hepatocytolytic serum (Brulé and Lemiere).

II. The Glycogenic Function.—Stoppage of the flow of bile has been supposed to prevent the storing of glycogen. Glycosuria has been observed in certain disorders of the liver, but as changes in the pancreas may also cause it, the occurrence of glycosuria does not prove that the trouble lies in the liver. The weight of opinion is that alimentary glycosuria is not a trustworthy test of hepatic insufficiency.

Sachs found that dehepatized dogs showed a lessened tolerance for levulose but not for dextrose, galactose, and arabinose. Clinically, he found that healthy as well as diabetic subjects have a greater tolerance for levulose than for dextrose, and that the subjects of hepatic disease have a lessened tolerance for a like amount of levulose. Strauss found that 90 per cent. of hepatic subjects presented levulosuria after the ingestion of a measured amount of levulose. His observations were confirmed by von Halász and Goodman. Alimentary levulosuria has been utilized as a test of hepatic insufficiency. Spence and Brett (1921) improved the

Sachs-Strauss levulose test by estimating the rise in blood sugar following oral administration of 50 gm. of levulose.

Alimentary levulosuria seems to be of special diagnostic significance in hepatic cirrhosis. It has not been found in many non-hepatic diseases; pneumonic subjects are said to exhibit both spontaneous and alimentary levulosuria, but these are not likely to be confused with diseases of the liver.

In connection with the glycogenetic functions of the liver, the experimental studies of Mann and his associates,[1] bid fair to prove that the liver has a vital function in relation to carbohydrate metabolism. Mann has shown that following the removal of the liver, a characteristic group of symptoms appears in orderly fashion as progressively diminishing levels of blood sugar are reached. The sequence is as follows: Muscular weakness, loss of reflexes, flaccidity, return and exaggeration of reflexes, muscular twitchings, convulsions and respiratory death in from five to eleven hours after removal of the liver. Mann found that these characteristic symptoms exactly paralleled the decreasing blood-sugar level following hepatectomy. Muscular weakness appeared when a blood-sugar level of usually 0.05 per cent. was reached, whereas convulsions occurred when the level of blood sugar decreased to 0.03 per cent. and death occurred shortly after. He also found that the glycogen content of the muscles decreased. He believes that the relationship of the decrease in blood sugar and the development of characteristic symptoms is one of cause and effect, for the injection of glucose intravenously would promptly revive such moribund dogs. They found that definite amounts of glucose for each kilogram of body weight would restore and maintain the dog for equally definite periods of time so that such animals could be repeatedly revived up to a maximum period of thirty-four hours following hepatectomy. Mann's experiments seem to indicate that the liver through its glycogenetic function is the dominant organ in sugar metabolism, and that the hepatectomized dog will remain normal until it has exhausted its maintenance level of blood sugar and has used up the glycogen previously furnished to the muscles by the liver, at which point the characteristic group of symptoms followed by death occur. The animal may be temporarily restored to normal, best by intravenous injection of glucose, less well by administration of glucose by jejunostomy, intraperitoneally, by mouth and by rectum. Out of 21 other related substances tested, only 4, maltose, mannose, dextrin and galactose were found to have a beneficial action but no one was so efficient as glucose. Their experiments emphasize the tremendous compensating power of the liver since they found that, if a very small part of liver tissue was left, the characteristic symptoms would not occur.

A further investigation of the effect of removal of the liver on the level of blood sugar was carried out on dogs in which previously the pancreas had been removed, in order to determine what might take place in a state of hyperglycemia. The liver and pancreas were removed at varying

[1] Mann, F. C.: *Am. Jour. Med. Sci.*, 1921, **161**, 37. Mann, F. C. and Magath, T. B.: *Arch. Int. Med.*, 1922, **30**, 73; *Ibid.*, 1922, **30**, 171; *Ibid.*, 1923, **31**, 797; *Am. Jour. Physiol.*, 1923, vol. **65**.

intervals in relation to each other. When the two glands were removed at the same time, the resulting condition was the same as though the liver only had been removed. When the liver was removed twenty-four to ninety-six hours after pancreatectomy, the blood sugar decreased quickly and the same characteristic symptoms developed as after hepatectomy, but at a higher blood-sugar level. The injection of glucose restored the animal to normal but the effect was more transitory. The total removal of the pancreas and the partial removal of the liver in an animal in which an Eck fistula had been made was followed by only slight or no increase in blood sugar. These experiments prove that the presence of the liver is necessary for the hyperglycemia following pancreatectomy.

As Banting and MacLeod have found that the administration of insulin produces a similar hypoglycemia with the development of a characteristic group of symptoms likewise relieved by the administration of glucose, a close similarity apparently exists between the effect of the removal of the liver and the administration of insulin.

Mann and Magath next studied the effect of intravenous injection of insulin on total and partial hepatectomzed dogs and found that the symptoms associated with the hypoglycemia following the administration of insulin did not differ essentially from the symptoms associated with the hypoglycemia following removal of the liver and the action of glucose seems to be identical in the two conditions. However, the hypoglycemia following the administration of insulin may not always be associated with symptoms, whereas the hypoglycemia following removal of the liver invariably produces symptoms. The effect of large doses of insulin producing hypoglycemia is not changed by total removal of the liver, nor is the hypoglycemic action of small doses of insulin modified by the partial (60 per cent.) removal of the liver. When the liver is totally removed, the blood-sugar level cannot be maintained normally. When the liver is partially removed, return to normal following insulin is greatly retarded. These experiments prove that the liver is certainly not necessary for the hypoglycemic action of insulin, although they do not show that it is not directly or indirectly involved in such an action. They definitely prove, however, that the liver is necessary for the permanent recovery of the blood-sugar level.

III. The Urea-forming Function.—The synthesis of urea from ammonia compounds and the availability of disturbances in this function as a test of hepatic insufficiency have also been much studied. *A priori* it is not unreasonable to suppose that if the activity of the liver be reduced the amount of urea in the urine should be diminished and that of ammonia increased. This has received some support from experimental studies, by means of Eck fistulas in dogs. In jaundice from obstruction the output of urea is usually not affected, although the percentage of ammonia is increased. In cirrhosis, on the other hand, the urea is diminished and the ammonia is much increased, which lends support to the theory of disturbed urea synthesis; but this theory is more or less discredited by the fact that feeding ammonia salts to cirrhotic subjects is not followed by impairment of the formation of urea. Stadelmann advanced the theory of acidosis, seeking to explain the increased ammonia output on the purely

chemical basis of the neutralization of an excess of acid. The volatile fatty acids have been found increased; sarcolactic acid and diacetic acid have also been found, which, in connection with lessening of the alkalinity of the blood and increase of bases in the urine (Münzer and Soetbeer), tends to confirm the theory of acid intoxication.

More recent work has advanced our knowledge of the urea-forming function of the liver. Among the most important have been the experiments of Mann and his co-workers[1] after complete hepatectomy. They studied the effect of total removal of the liver on the formation of urea in more than 90 hepatectomized dogs and found that the production of urea in the body of the dog is entirely dependent on the presence of the liver, since urea formation ceases completely as soon as the liver is removed, with a coincident progressive decrease of urea in the urine and an increase in the amino-acid content of the blood. Furthermore, they found that the destruction of uric acid in the normal dog depends on the presence of the liver since this process ceases as soon as the liver is removed, with coincident increase in the uric acid content of the blood and appearance in the urine of large amounts of uric acid. That the latter is not due to increased production of uric acid is suggested by the fact that there is no increased nitrogen excretion. The creatin-creatinin metabolism is not affected by removal of the liver. Mann's experiments seem to show that there is dissociation of the process usually called "protein metabolism." While there appears to be no question that the greater portion of this prócess depends on the action of the liver, it is not alone concerned with all phases of it. It is certain, however, that protein metabolism does not occur as an orderly process without the liver (Mann).

Stadie and Van Slyke[2] studied the blood chemistry and urine in a case of acute yellow atrophy of the liver and their observations support the conclusions that due to the autolysis of liver cells in the rapidly atrophying liver, the amino-acids formed are excreted in the urine (leucin and tyrosin); that their excretion appeared due to loss of power on the part of the liver to deaminize rather than to production of large amounts of the amino-acids; and that the aminization and synthesis of urea cannot be entirely assumed by extrahepatic tissues. This is consistent with clinical observations which show that in serious liver disease, with destruction of the liver cells by fatty degeneration, acute autolysis or necrosis, or by pressure on liver cells from connective tissue overgrowth, as in acute yellow atrophy, phosphorus poisoning and certain forms of cirrhosis, there is a decrease in the amount of urea in the urine, but an increase of its ammonia content.

IV. The Detoxifying Function.—There is an increasing amount of evidence indicating that the liver is capable of destroying many toxic substances but also evidence that in the long-continued fixation of these injurious substances, progressively destructive changes in liver tissue take place.[3]

[1] Bollman, Mann, Magath: *Am. Jour. Physiol.*, 1924, **69**, 371.

[2] *Arch. Int. Med.*, 1920, **25**, 693.

[3] Excellent reviews with extensive bibliographies have been published by Gunn, J. A.: *Physiological Reviews*, 1923, **3**, on congenital and acquired tolerance of non-protein substances, and by Opie, *Jour. Am. Med. Assn.*, 1925, **85**, 1533, on the physiology of the liver in relation to intoxication and infection.

Certain substances highly poisonous when administered hypodermically are much less harmful or entirely innocuous when administered by mouth. In some cases, this detoxification seems to be brought about by the gastric and intestinal secretions, but in many cases poisons are carried by the portal circulation to the liver and there deprived of their toxicity. This obtains in the case of substances such as curare, nicotine, and to a less extent, substances such as morphine, strychnine, alcohol and atropine. Certain toxic substances seem to have a selective affinity for the liver, producing a widespread fatty degeneration (phosphorus) or acute cellular necrosis (chloroform). Williamson and Mann[1] caution against drawing conclusions as regards the functions of the liver from studying the effects of chloroform, phosphorus and allied poisons, since they found in comparing the effects of such administration with those following total removal of the liver, that while such poisons greatly injure the functions of the liver, they do not produce the complete picture of hepatic insufficiency (lethal hypoglycemia, appearance of uric acid, cessation of urea formation, and the production of the characteristic symptoms). The liver is believed to exert a similar detoxifying action on the toxins of certain bacteria and on the products of bacterial putrefaction in the intestine, such as indol, skatol and phenol. In some cases, these poisons are excessive in amount or in virulence and the liver is unable to handle them. Disturbances in this protective or detoxifying function of the liver are believed to be the basis of the eclamptic manifestations of uremia, pregnancy, etc. There is no doubt that in disease the detoxifying function of the liver becomes more or less impaired, but there are no trustworthy diagnostic tests of this function.

Minute particles of insoluble substances capable of passing through the bile capillaries are bound within the liver by the phagocytic action of certain of its cells, particularly the cells of Kupffer, which according to Opie and others, play an important part in the fixation of inorganic particles, bacteria, colloid material, and possibly substances dissolved within the plasma. Certain cells of the spleen and of the lungs are likewise capable of ingesting these various substances but in less amounts than cells within the liver. Drinker and Shaw demonstrated that the liver is the organ chiefly concerned in removing insoluble particles from the blood. They particularly studied manganese and found that 90 per cent. was recoverable from the liver, lungs and spleen, and that gradually the liver absorbed the manganese from the lungs. The greatest amount was found within the Kupffer cells which are evidently the most effective agents in removing it from the circulation. Carbon particles entering the blood stream are found within the liver and anthracotic pigmentation of the liver is often found in advanced pulmonary anthracosis. Cirrhosis of the liver may also occur.

There seems to be some selective activity on the part of the lobes of the liver to fix particulate matter brought to it in the portal blood. For instance, after injecting India ink into the splenic vein the deposition of such pigment is found largely within the left lobe, whereas the same sub-

[1] *Am. Jour. Physiol.*, 1923, **65**.

stance injected into the superior mesenteric vein will be found deposited largely in the right lobe of the liver (Riemann). Instead of indicating a selective activity of liver lobes, this may be due to the mechanics of the current of circulation of blood in the splenic trunk of the portal vein. Bartlett[1] and his associates from their experiments on dogs believe that there is a physiological independence of the lobes of the liver, depending upon the fact that the blood flowing into the portal vein from each of the smaller veins of the portal system, does not blend diffusely into a common current, but remains individualized to a considerable degree, streaming in thread-like currents, for distances varying up to 10 cm. Depending upon this principle, they found by injection of emulsified fat in the various portal tributaries, and by the absorption of copper from the various isolated intestinal segments that: (1) Blood from the stomach, spleen, duodenum, first part of the jejunum and from the rectum flows mainly to the left lobes of the dog's liver and least to the right lobes; (2) blood from the lower jejunum, ileum and first part of the large intestine flows principally to the right lobes of the liver and least to the left lobes; (3) this independence is not entire, but overlapping, due to an intermixing of the portal currents; (4) the currents of blood from the splenic and rectal veins, are, at the hilus of the liver, more sharply defined than the currents of blood from the ileal veins which must flow a greater distance in the portal vein to reach the hilus of the liver, and consequently become more mixed and less independent.

This seems to throw additional light upon the clinical association between enlargement of the left lobe of the liver in certain splenic diseases (such as Banti's disease, hemolytic jaundice with splenomegaly, etc.) and the hepatitis and resulting cirrhosis that occurs as a result of chronic focal infective disease of the appendix, duodenum and gall-bladder.

V. Bactericidal Function.—The healthy liver seems to possess the power of destroying or rendering harmless bacteria which enter the body by way of, or are elaborated within, the gastro-intestinal tract. It aids in destroying bacteria entering by way of the circulating blood. Many experiments have shown that the liver exerts an important function of removing bacteria from the blood stream. The lung and spleen likewise participate in this function but from its large size and great vascularity, the liver is predominant. Furthermore, it is so situated in relation to the portal circulation that it can take up bacteria which under normal or pathological conditions have passed through the intestinal wall and thus prevent their entrance into the systemic circulation. The cells of Kupffer again appear as the most active phagocytic cell although other cells of the liver participate. The bactericidal power of the liver increases with immunization and the phenomenon of agglutination is not essential to the fixation of bacteria. As in other functions of the liver, long-continued assaults tend to wear down the cellular bactericidal power, and degenerative changes, and later destructive cellular lesions, develop. The observations of many workers have demonstrated that in bacterial focal infections of the appendix, in duodenal (ulcer) and gall-bladder infections, as well

[1] Bartlett, Corper, and Long: *Am. Jour. Physiol.*, 1914, **35**, 36.

as in the intestines themselves (colitis), the liver becomes chronically inflamed and cellular destruction gradually occurs. Sections from the liver removed at operation for the other lesions show well-developed hepatitis in the acuter cases and various grades of hepatitis plus cirrhosis in the more chronic cases. The increased bactericidal power of the liver after immunization has been clinically suggested in patients by the observations of Lyon, Bartle and Ellison,[1] who found that the use of autogenous vaccines made from cultures of bile, with duodeno-biliary tract drainage made it impossible to recover further viable cultures from the bile after a few months. There was a coincident arrest in symptoms. That the bacteria originally recovered from bile cultures often possessed a selective affinity for the liver, gall-bladder and ducts was proved by Kolmer.[2] The Heist-Lacey test for the bactericidal power of the blood serum after such use of vaccines and drainage of the liver shows similar evidence of improvement. The power of the liver to protect the body against the effect of foreign protein was suggested in 1906 by the experiments with egg-white injected intravenously (Chiray, Langar). More recently, Falls[3] and Manwaring and Crowe[4] have shown that the liver of a sensitized animal can destroy the toxicity of foreign protein. Their experiments suggest that the action of the liver upon foreign protein is analogous to its action on bacteria, for in both instances the organ diminishes the injurious effects of the foreign substance and in both instances the protective action is increased as a result of the immunization. It is not improbable that the liver acts in the same way upon many injurious bacterial products which, like proteins, act as antigens and induce immunity (Opie).

VI. The Lipogenetic Function.—In health, the warehousing of fat in the liver is a function of less importance in man than in some of the lower animals, especially those that have little power to accumulate fat in the muscles and other tissues. In diseases, however, the liver may store considerable fat, but only when the amount of stored glycogen becomes much decreased or disappears. Disturbances of fat metabolism may be attended by extremely serious consequences, notably the condition spoken of as ketosis. Although formed from the fats of the body in certain conditions when the oxidizing powers are reduced, they are directly related to deficiency of glycogen, which may be the consequence of insufficient intake (as in starvation) or of excessive output (as in diabetes).

VII. Liver Function in Iron Metabolism.—Rous and Oliver after injecting blood into rabbits over long periods, found an immense deposit of iron-containing pigment fixed within the liver. The spleen undergoes enlargement and its phagocytic cells contain erythrocytes which gradually break down into hemosiderin. The spleen for a time holds the hemosiderin and thus protects the liver until its capacity to store it is overcome, when the iron is deposited in the phagocytic cells (chiefly the Kupffer cells) within the sinusoids, especially at the periphery of the lobule. The cells

[1] *Am. Jour. Med. Sci.*, 1922, **163**, 60 and 223.
[2] "*Non-surgical Drainage of the Gall Tract*" (Lyon), Lea & Febiger, 1923, p. 353.
[3] *Jour. Infect. Dis.*, 1918, **22**, 83.
[4] *Jour. Immunol.*, 1917, **2**, 517.

of the cortex of the kidney take up the hemosiderin later and the cells of the pancreas still later. Thus iron metabolism (participated in by the liver), if disturbed, produces changes closely resembling hemochromatosis. Whipple points out a possible relationship between pernicious anemia and hemochromatosis in that they both have a definite over-production of pigment in the body but a different rate of increased destruction of hemoglobin and erythrocytes. Furthermore, Mallory and his co-workers,[1] have recently suggested that a common cause of cirrhosis of the liver may lie in the continued ingestion of foods cooked in copper-lined kettles. They found that giving 2 gr. (0.1 gm.) of acetate of copper daily over a period of months, produced changes in the liver similar to those of hemochromatosis in man, finally causing cirrhosis, but without anemia. Disturbance of iron metabolism appears to be brought about by the strong affinity of copper for hemoglobin, with resulting formation of cuprohemol. This accumulation of iron-containing pigment in large quantities within the liver and other tissues gradually producing cirrhosis, seems to represent an abnormal process of pigment formation and destruction and appears in part referrable to hepatic functions concerned with the formation of bile pigment. In any event, the formation of bile pigments is associated with the capacity of the liver to select and fix certain iron-containing substances which are normally present in the blood stream.

LIVER FUNCTIONAL TESTS

In an organ so difficult of direct examination, the use of indirect methods is necessary. Aid in investigation has come from the use of the duodenal tube and the methods for studying duodenobiliary-pancreatic aspirates. The direct study of the bile is an additional means of estimating disease of the liver, gall-bladder and ducts,

It is probable that no liver function test as yet introduced is capable of accurately estimating in a total sense the degree or extent of actual damage that has taken place in the liver, nor can an altogether accurate impression be gained as to just *which* function is most seriously impaired. This is largely due to the fact that the liver has a tremendous margin of safety, can tolerate extensive injury and still retain its power to regenerate impaired cells and because its functions may overlap or interlock. Some functions may be seriously impaired while others of more fundamental importance do not appear deranged. It is evident, therefore, that any single test of hepatic function as yet devised is inadequate for the testing of all functions of the liver, yet, by combining several of them, a very definite impression of hepatic cellular damage or functional deficiency may be gained.

I. The *van den Bergh Test.* – The diazo reagent of Ehrlich is used as a means of detecting bile pigment in blood serum. Two types of reaction occur, the direct and indirect. The *direct reaction* may be divided into (*a*) a prompt reaction, (*b*) a delayed or negative reaction, and (*c*) a biphasic reaction. A prompt direct reaction indicates obstructive jaundice

[1] Mallory, Parker, and Nye: *Jour. Med. Research*, 1921, **42**, 461.

involving chiefly the common duct (stone, tumor, etc.). The delayed direct reaction is suggestive of the hemolytic form of jaundice of various types. The biphasic reaction occurs most frequently with toxic and infective forms of jaundice.

As regards the *indirect reaction*, van den Bergh showed that normal blood serum contains a small amount of bilirubin in values ranging from 1 in 1,000,000 to 1 in 400,000. For quantitative determination, van den Bergh takes as his unit of bilirubin, the figure 1 in 200,000. Therefore, 0.2 to 0.5 of a "unit" is the normal figure or an average of 0.3 of a unit. When the bile pigment rises above this normal of 1 unit, various pathological states of liver or bile-tract disease may be inferred to exist. Even apparently healthy individuals of a sallow complexion may be found to have bilirubin as high as 1 in 80,000 or 3 units and represent a so-called "latent" form of jaundice, without biliuria. Bile from the gall-bladder always gives a prompt direct reaction. Bilirubin from hemorrhagic exudates into serous cavities give delayed reactions only. The *renal threshold* for bilirubin excretion is the variable modifying the appearance of biliuria. For instance, in latent obstructive jaundice with absence of biliuria there will usually be found less than 4 bilirubin units, whereas in latent hemolytic jaundice, more than 4 units may be found, as in pernicious anemia and also in the serum of newly-born babies. In these conditions the delayed reaction only occurs. On the contrary, in the latent jaundice of cirrhosis or metastatic cancer, a prompt direct reaction, but of low values, will occur, Latent jaundice also exists in syphilitic disease of the liver and when detected by the van den Bergh test may presage that a frank jaundice will follow arsenical treatment (Gerrard). The French authors (Brault and Garban) recognize a latent jaundice when bile salts and urobilin are present in the urine but bile pigment is absent, (so-called "dissociated "jaundice).

The *biphasic reaction* is taken to mean that there are two kinds of bilirubin present in the serum, one giving the prompt reaction only, and the other the delayed reaction, depending upon the degree of damage to the liver cells and the degree of obstructive cholangitis, but presupposing that both of these factors are involved, as in toxic or infective jaundice. The exact nature of the difference in these two kinds of bilirubin is not known. In cholelithiasis, without jaundice, the bilirubin content of the serum is normal unless involvement of the liver or ducts has occurred. The condition "dissociated jaundice" of the French school remains to be investigated by the van den Bergh test and it may be safer to defer judgment as to its clinical frequency and importance (McNee).

Among various modifications of van den Bergh's test might be mentioned those of Blankenhorn,[1] Fouchet,[2] Meulengracht,[3] Haselhorst,[4] and Thannhuaser and Andersen.[5] Holzer and Mehner[6] have comparatively tested these modifications and consider van den Bergh's test the most reliable.

[1] *Arch. Int. Med.*, 1917, **19**, 344.
[2] *Compt. Rend. Soc. de Biol.*, 1917, **80**, 826.
[3] *Deutsch. Arch. f. klin. med.*, 1921, **137**, 38.
[4] *Muench. Med. Wchnschr.*, 1921, **68**, 174.
[5] *Deutsch. Arch. f. klin. med.*, 1921, **137**, 179.
[6] *Klin. Wchnschr.*, Berlin, 1922, **50**, 66.

II. Bernheim[1] has developed a method of colorimetrically estimating quantitatively the amount of bile pigment in the blood serum, by means of which test the "icterus index" is determined. The normal icterus index lies between 2 and 5; in cases of clinical icterus the index reaches 15 or above; when clinical jaundice is absent, the index falls below 15. Therefore, the zone of latent jaundice ranges between 6 and 16. The normal bilirubin content of the serum is 1 part in 500,000. Clinical icterus becomes evident when the bilirubin content reaches 1 part in 50,000. Between these two levels lies the zone of latent jaundice. The pigment serum has been found quantitatively increased and the "icterus index" therefore higher (6 to 20) in (*a*), disturbances of the biliary system such as cholangitis, cholelithiasis, cholecystitis, adhesions to gall-bladder or liver involving the bile ducts, hepatitis, cirrhosis and cancer of the liver, and (*b*) in hemolytic jaundice, hematomas, a ruptured viscus, with blood extravasation, and in cardiac decompensation, pneumonia, malaria and typhoid fever. It is probable that the icterus index is the most useful single functional liver test for general clinical work.[2]

III. Rosenthal and White[3] studied the intravenous introduction of "bromsulphalein" (phenoltetrabromphthalein sodium sulphonate) as an indicator of hepatic function. This method does away with several of the disadvantages attendant upon the use of phenoltetrachlorphthalein. Bromsulphalein has been standardized for clinical use as a test for hepatic function based on the rapidity of its removal by the liver from the blood stream. Normally, following the intravenous injection of 2 mg. of the dye per kilogram of body weight, it is completely removed from the blood in thirty minutes. In liver disease it is retained in the blood in concentrations that vary from 0 to 100 per cent. of the amount injected. The percentage of the dye present in the serum thirty minutes after injection expresses directly the degree of impaired liver function. It is claimed that this new dye is non-toxic in the dosage employed and is non-irritating to the vein wall.

Among dye tests, basing an estimation of hepatic function on the ability of the liver to withdraw from the blood stream dyes introduced intravenously, Rosenthal's test has received the largest measure of endorsement. In a comparative study of liver function tests, Greene found that in various diseases of the liver, with and without jaundice, the accuracy of interpretation in terms of the degree of dye retention, was closely parallel to that with the van den Bergh test.

Among additional dye tests, Aaron, Beck and Schneider[4] and later Piersol and Bockus[5] tested out the bile content of phenoltetrachlorphthalein injected intravenously to determine the ability of the liver to excrete this dye. They found that with normal hepatic secretory function, the dye passed through the liver and could be detected in the bile obtained by duodenal tube in from twelve to seventeen minutes; whereas

[1] *Jour. Am. Med. Assn.*, 1924, **82**, 291.

[2] Consult Stetten: *Ann. Surg.*, 1922, **86**, 191; Barrow, Armstrong and Olds, *Am. Jour. Med. Sci.*, 1925, **169**, 583, and 1925, **170**, 519; Shattuck, Browne and Preston, *Am. Jour. Med. Sci.*, 1925, **170**, 510; and O'Leary, *Med. Clin. North America*, 1925, **8**, 1203.

[3] *Jour. Am. Med. Assn.*, 1925, **84**, 1112.

[4] Ibid., 1921, **77**, 1361.

[5] *Arch. Int. Med.*, 1923, **31**, 623.

in various diseases in which the liver was functionally deranged or organically damaged, the appearance-time of the dye was distinctly delayed and its quantitative elimination greatly decreased. This was a modification of the original method of Rowntree and his associates who introduced this dye as a test for liver function, but estimated the amount excreted by the liver by testing the amount of dye elimination in the stools. Inasmuch as many dyes are excreted in large part by the kidneys as well as the liver, Tada and Nakashima[1] after a study of 62 dyes found that Azorubin S was eliminated 95 per cent. by the liver and 5 per cent. by the kidneys and they consider it the ideal dye for testing this phase of liver function. They used the duodenal tube to determine the time-rate of excretion of this dye in the bile and find that in normal persons, it appears in seventeen minutes, whereas in clinical states of liver disease its appearance-time is delayed.

IV. Investigating *bile pigment metabolism*, and its relation to liver function, Jones[2] studied a series of cases both by estimating the amount of bilirubin in the serum and bilirubin in the bile recovered by duodenal aspirates. He found that in the hemolytic diseases, such as pernicious anemia, there was a definite increase in retained bilirubin in the plasma and bilirubin excreted in the bile. Likewise in a series of cases of liver disease, including cancer, cirrhosis, and toxic and infective hepatitis, there was also a definite increase in bile pigment in both blood serum and the bile itself, much beyond that found in normal persons. In gall-bladder disease, subsequently proved by operation, there was also an abnormally high concentration of bile pigment in the bile and blood serum, cases of cholecystitis alone showing higher concentrations than found in cholelithiasis, suggesting that the concentrating function (Rous) of the gall-bladder was more seriously impaired. He believes that the high level of bile pigment found in pernicious anemia is not due alone to increased blood destruction, but indicates also an alteration in hepatic function.

V. *The Sachs-Strauss Levulose Test* (modified by Spence and Brett).—This test originally consisted of giving 100 gm. of levulose by mouth and collecting urine for examination. If sugar appeared in the urine, hepatic insufficiency was thought to be present. Spence and Brett[3] found that the kidney threshold for levulose is lower than for glucose and varies greatly in individuals, rendering inaccurate the test of liver efficiency by urinary examination alone; in some normal cases 50 gm. of levulose gave glycosuria whereas in some cases of known liver disease glycosuria did not appear. They modified the test by a method which excludes kidney interference. They estimate the changes in blood-sugar concentration following the ingestion of levulose. In healthy adults with normal liver function, 50 gm. of levulose by mouth will produce no definite rise in blood sugar, whereas in patients with liver damage it will produce an appreciable rise in blood sugar. The height and duration of this increased blood-sugar curve they believe indicates the degree of liver insufficiency present. They find it of particular value in cases of cirrhosis and toxic

[1] *Jour. Am. Med. Assn.*, 1924, **83**, 1292.
[2] *Arch. Int. Med.*, 1922, **29**, 643.
[3] *Lancet*, 1921, ii, 1362.

or infective hepatitis. This test is considered to give evidence of acute liver damage with or without jaundice. The original levulosuria test was positive in most cases of early jaundice except of the hemolytic variety.

VI. There are certain inferences in regard to hepatic dysfunction or insufficiency which can be drawn from the study of the bile obtained by biliary-tract drainage. Where the microscopic examination discloses large amounts of various crystals, cholesterol or bile pigment, or calcium, it may indicate that the bile is merely supersaturated and unable to hold such crystals in solution, or it may indicate some inability on the part of liver cells to elaborate a bile of normal crystalline content. This constitutes a condition of "potential lithiasis" and is a common finding in patients with gall-stones. It is important, however, in recognizing the gall-stone carrier, to examine the bile over a period of several days to exclude the factor of a diet rich in cholesterin or calcium producing qualities.

When an excessive amount of lecithin or leucin or tyrosin appears in the slides, it is suggestive that more serious, though perhaps only temporary, damage to the liver cells has taken place, impairing their ability to properly synthesize these elements. Clinically, leucin and tyrosin are found in the urine in association with certain fevers which are thought to impair liver function, such as typhoid fever. When an unusual amount of hippuric or uric acid crystals appear, it suggests the possibility that the liver function is deficient in its ability to destroy uric acid as determined by Mann's experiments. In many cases of liver disease, as well as gall-bladder and duct disease, excessively large amounts of bile salts are found. Their significance is not yet clear.

When numerous bile-stained colonies of bacteria or enormous numbers of bile-stained bacteria appear diffusely throughout all fields and such bacteria are culturally viable, a deficiency in the bactericidal power of the liver is suggested. The finding of bile-stained colonies of bacteria makes it appear likely that at some point within the biliary tract bacteria have obtained lodgment and represent a focal point of infection.

By bile-tract drainage, one also gains an impression as to the bile secreting function of the liver and whether or not the larger ducts are partly obstructed or the smaller intrahepatic duct radicals are choked by "biliary thrombi," suggesting that the obstruction to free bile secretion lies within the liver itself. The observations as to the rate of bile flow, abnormal pigment concentration of the "C" bile or increased viscosity, the point during the drainage at which the catarrhal flocculi appear, and their microscopic features, are important evidence. Although the gall-bladder possesses the greatest power of concentration of bile, when either the extra- or intrahepatic ducts are dilated, increased concentration of duct bile will occur. If the mucus flocculi are coming from the common duct they are usually coarser and thicker in outline than the finer flocculi which come down at a later point in drainage, being apparently washed out from the smaller intrahepatic ducts; and the columnar epithelium lining them, when exfoliated, will be found much shorter. The rate of delivery of bile is necessarily more slow when catarrhal or

crystalline obstructive features exist. Not infrequently, gall-stone sand is recognizable. In certain states of liver disease, more commonly in the cirrhoses, without catarrhal duct obstruction or visible jaundice, the rate of bile secretion may be unusually rapid.

VII. Among other tests of liver function might be mentioned that of Widal. The Widal hemoclastic crisis test[1] is based on the assumption that the digestive leukocytosis noted after food ingestion is due, in part, to liver participation. Widal claims that in diseases of the liver, this normal digestive leukocytosis does not occur, but is replaced by a leukopenia. This test has been studied by numerous observers who in large part fail to support its value.

JAUNDICE

Jaundice is a term applied to staining of the tissues with bile pigments present in the blood. It is recognized clinically by a yellowish or yellowish-green discoloration of the skin and visible mucous membranes and by the presence of bile pigments in the urine. It is not a disease *sui generis*, but a feature of a wide variety of disorders. Although it indicates some disturbance in the secretion or excretion of bile, and is, therefore, significant of disease of the liver, it occurs also in disorders in which the liver is not involved primarily.

Jaundice occurs in a variety of circumstances. In many cases it results from an obstruction to the free flow of bile. Often the obstruction is obvious and consists of: (1) An obstruction within the common bile duct or the hepatic duct, such as gall-stones, parasites, foreign bodies, etc.; (2) inflammatory, cicatricial, or neoplastic stenosis of the ducts; (3) compression of the ducts from without by tumors of the pancreas, stomach, intestine, gall-bladder, regional lymph glands, kidney, retroperitoneum, mesentery, etc., inflammatory adhesions, swollen glands, fecal accumulations, aneurism of the aorta or of the hepatic or mesenteric artery; or (4) kinking or torsion of the ducts in consequence of gastroptosis, hepatosis, nephroptosis, the pregnant uterus, tumors of the abdominal or pelvic organs, etc. In another series of cases—of disease of the liver unattended by gross obstruction of the extrahepatic biliary ducts—the hindrance to the free flow of bile is none the less demonstrable, if less marked and less obvious at first sight; these comprise cases of localized inflammatory processes (abscesses), tubercles, gummas, hydatid cysts, primary and secondary new growths within the substance of the liver, etc. Jaundice, however, occurs under other circumstances in which apparently the biliary ducts are patent, as in cirrhosis and other diffuse diseases of the liver; in many infections, such as the different types of so-called infectious jaundice, syphilis, yellow fever, septicopyemia, malaria, pneumonia, typhoid fever, etc.; in intoxications, such as poisoning with phosphorus, arseniuretted hydrogen, chloroform, mushrooms, toluylendiamin, pyrogallol, snake venom, coal-tar products, etc.; in acute yellow atrophy of the liver; in pernicious anemia and hemoglo-

[1] Widal, Abrami and Jamcovesco: *Compt. Rend. hebdom des seances de l'acad. des sciences*, 1920, **181**, No. 5.

bilemia, and in disturbances of the circulation, such as passive congestion; in the new-born, etc.

Types of Jaundice.—There has been much confusion as to a proper classification of jaundice and McNee has suggested a simplification of terms. He classifies all forms of jaundice under the headings of (1) obstructive hepatic jaundice, (2) toxic and infective hepatic jaundice, and (3) hemolytic jaundice. Such a classification is both simple and practical.

1. *Obstructive jaundice* may be produced in a variety of ways, as described on page 731.

2. *Toxic and Infective Hepatic Jaundice.*—This may occur in a wide variety of conditions and is the commonest type seen clinically. It occurs: (*a*) as a complication of many acute infections such as typhoid fever, pneumonia, yellow fever or spirochetal jaundice; (*b*) accompanying many general conditions of infection or toxemia, such as in acute septicemia, uremia, or in cardiac decompensation, producing chronic passive congestion; (*c*) after the administration of certain products, such as phosphorus, chloroform, arseno-benzol compounds, trichlorethane, trinitrotoluene; or experimentally after arseniuretted hydrogen, phenylhydrazine, etc.; and (*d*) after damage to liver cells from an unknown source. Here may be grouped the jaundice of acute yellow atrophy or necrosis of the liver, and the severe degenerative autolytic changes in the liver embraced within the term icterus gravis.

3. *Hemolytic Jaundice.*—Here may be included: (*a*) chronic splenomegalic hemolytic jaundice, particularly the hereditary form; (*b*) the jaundice accompanying pernicious anemia, and perhaps various anemias associated with parasitic diseases; and (*c*) icterus neonatorum.

Groups (*b*) and (*c*) fall within the category of a new form of jaundice called *latent jaundice*, recognizable by means of the van den Bergh test. They give the delayed or absent direct reaction accompanying hemolysis, rather than the prompt direct reaction due to obstruction.

Dissociated Jaundice.—There is still another form of jaundice described by the French which they call "dissociated" jaundice.[1] Widal, Lemierre, Garban, Abrami, Brulé and others emphasize the factor of functional disorder of the liver cell as quite as important in the production of jaundice as obstruction of the small bile ducts. They contend that in many of the cases classified as toxic or infective jaundice, the liver cells are damaged and the function of normal secretion of normal bile is particularly impaired. They found that in many such cases, the bile pigments and bile salts excreted in the urine are "dissociated," one being retained and one excreted; often bilirubin is present in the urine, but bile salts are absent. They point to the fact that in the jaundice of typhoid fever white bile, rich in bile salts, is found in the gall-bladder. They state that bile pigment retention, with normal excretion of bile salts in the urine, is common in catarrhal jaundice, while the stools are still clay-colored. Whereas, in cirrhosis of the liver, retention of bile salts and normal excretion of bile pigment will be observed, accompanied by skin

[1] For a complete review of this subject, consult Brulé, M., *Recherches sur les Icteres*, Paris, 1922, 3d edition.

itching and bradycardia. They show, on the contrary, that in true obstructive jaundice, due to blockage of ducts, both bile pigments and salts pass into the blood and are excreted by the kidneys. This represents to them "complete jaundice." Brulé therefore claims that the presence of "dissociated" jaundice indicates that the cause of such jaundice is in disordered function of liver cells and not to obstruction. While many of the French arguments are attractive, they have not been fully accepted. For instance, Hoover and Blankenhorn[1] insist that the blood as well as the urine should be examined before "dissociated" jaundice can be proved. On studying the subject from this angle, they have never found the bile pigment without the bile salts in the blood plasma except in 2 cases of primary anemia and in 2 cases of lead poisoning. These, therefore, might be considered true dissociated jaundice. In addition, they summarize their study as follows:

1. Excepting in jaundice of hemolytic origin and in complete jaundice which has undergone renal dissociation, we have never found bile pigment without bile salts in the plasma.

2. Bilirubin and bile salts may both be present in very marked concentration in the plasma and neither pigment nor salts appear in the urine.

3. Adsorption of bilirubin in the plasma may not only withhold the pigment from the renal filter, but also from the tissues; so there may be pronounced cholemia (pigmental) without choluria (pigmental) and also without icterus of the tissues.

4. When pigmental cholemia is present (in varying degrees) without choluria, the collodion sack will yield no pigment to an aqueous dialysate from the plasma. When choluria attends cholemia (pigmental), the collodion sack will yield bile pigment to an aqueous dialysate from the plasma.

5. Bile salts will dialyze from plasma when no bile salts are demonstrable in the urine.

6. Without an examination of the plasma we are never justified in assuming that biliary elements have not been retained in the blood.

Blankenhorn[2] believes that if both blood and urine are carefully studied, "dissociated" jaundice will appear at sometime or other in practically every case of jaundice and that the dissociation of bilirubin and bile salts may be due to the excretion of bile salts only by the kidney. The difficulty will be clarified by the use of the van den Bergh test for bile pigment, and until then the importance and frequency of a true dissociated jaundice must be left unsettled.

Inasmuch as the etiological factor in many cases of so-called non-obstructive jaundice is unknown, it is difficult to differentiate them clinically or otherwise, aside from the severity of the symptoms; but the designations, mild and severe, are often inappropriate, since the degree of the jaundice and the severity of the other symptoms frequently bear no relationship the one to the other. There can be little question that many of the cases represent only different stages or grades of the one process. In a simple and usually mild form, jaundice is an accompaniment

[1] *Arch. Int. Med.*, 1916, **18**, 289.

[2] Ibid., 1918, **21**, 282.

or sequel of gastro-intestinal catarrh; the direct cause of the jaundice is an extension of the catarrhal process to the diverticulum of Vater or the common bile duct and consequent obstruction to the flow of bile. Since these cases commonly pursue a benign course, and the few that have come to necropsy have revealed only catarrhal papillitis or cholangitis, the disorder is spoken of as simple or catarrhal jaundice (preferably catarrhal cholangitis). Although rarely or never producing death, so-called simple catarrhal jaundice is fraught with considerable danger. Damage done to hepatic and pancreatic cells by pressure from dammed-up bile and pancreatic secretion (during the period of obstruction) may encourage the development of degenerative lesions, such as cirrhosis or diabetes (Lyon). The longer the obstruction remains the greater the potential damage, hence any treatment, such as biliary-tract drainage, which tends to release or dislodge the minute biliary thrombi or the catarrhal plugs of mucus from larger ducts, will materially shorten the duration of jaundice and protect against pressure damage to liver and pancreas cells.

In another series of cases in addition to the jaundice there are phenomena of general infection, such as fever, neuromuscular pains, enlargement of the spleen and liver, gastro-intestinal disorders, such as vomiting and diarrhœa, nervous manifestations, such as headache, stupor, etc., often leukocytosis, albuminuria, tube casts, etc.; to these cases the term infectious jaundice has been applied. The not uncommon epidemic occurrence of such cases warrants the use of the term epidemic jaundice.

Cockayne[1] states that catarrhal jaundice is the sporadic or endemic form of what he calls epidemic catarrhal jaundice, in the majority of cases. He also believes that in addition to sporadic and epidemic catarrhal jaundice, acute yellow atrophy is usually due to the same cause, a specific organism of unknown nature. In other cases the clinical phenomena are more severe, symptoms attributable to hepatic insufficiency, to poisoning by bile acids (cholemia), or to hepatic intoxication (acidosis), supervene, and a fatal issue usually ensues; the condition is spoken of as grave jaundice (icterus gravis). When, in addition, considerable destruction of the liver cells occurs, the term acute yellow atrophy of the liver is employed. No sharp line can be drawn between the cases; mild in the beginning (seemingly catarrhal jaundice), they may progress to the most severe and fatal form (acute yellow atrophy); the degree of jaundice bears no constant relationship to the demonstrable changes in the liver, nor to the severity of the other phenomena; in some cases of unusual and widespread destruction of the hepatic parenchyma the jaundice may be slight, rarely even entirely absent, so that, until the etiological factors are better elucidated, we must rest content with the terms toxic, infectious hemolytic, or hemohepatogenous jaundice, as seems best suited to specific cases. Some of the cases are unquestionably examples of bacterial infection of the biliary tract. Other cases, toxic in nature, result from poisons transported to the liver by the portal circulation. In still other cases the primary action of the poison is on the erythrocytes (hemolysis), in consequence of which an increased amount of free hemoglobin results in larger amounts of bilirubin.

[1] *Quart. Jour. Med.*, Oxford, 1912, **6**, 1.

Pathogenesis of Jaundice.—The mechanism of jaundice due to gross obstruction of the extrahepatic biliary ducts, or less marked obstruction of the larger intrahepatic ducts, is readily comprehended. On the one hand, the outflow of bile into the duodenum is hindered; on the other hand the hepatic cells, if normal, even after the common bile duct has been completely occluded, continue to secrete bile (although perhaps in lessened amount). In consequence of obstructed outflow and of continued production, bile accumulates within the biliary tract, the pressure increases, and the biliary ducts become dilated. It was demonstrated by Eppinger[1] that this dilatation extends to the finest biliary capillaries, which become enormously distended, especially at the points of communication of the capillaries of adjacent rows of liver cells. Furthermore, evidences of the increased pressure are seen in the intercellular biliary capillaries, which become lengthened in the direction of their distal end, dilate ampulla-like, and gradually approach and finally rupture into the lymph spaces between the hepatic cells and the bloodvessels; thence, by the thoracic duct, the biliary constituents reach the bloodvessels. That one pathway of the bile to the bloodvessels is by the lymphatics and the thoracic duct has been repeatedly demonstrated.

The mechanism of jaundice not due to obvious or gross obstruction of the biliary ducts is not so well understood. Frerichs believed that the bile found its way directly into the bloodvessels in consequence of changes in the tension of the contents of the hepatic cells and of the bloodvessels—either an increase in the intercellular pressure or a decrease in the portal pressure. Leibermeister believed that the disordered liver cells lost their ability to retain or fix the bile, and in consequence it became diffused into the bloodvessels or lymphatics. Minkowski assumed a disturbance in the normal currents within the liver cells, so that the bile became diverted from the biliary capillaries to the bloodvessels or lymphatics—jaundice from parapedesis (paracholia of Pick). The toxic and infectious causes of this form of jaundice compromise the functional integrity of the liver cells; but it has also been demonstrated that they provoke a radicular cholangitis which obstructs the free flow of bile. In these cases thrombi made up of coagulated bile occur in and obstruct the biliary capillaries; mechanical stasis of the bile develops in the finest biliary capillaries, and, as in cases of gross obstruction of the larger extrahepatic ducts, the biliary canaliculi dilate and ultimately rupture into the pericellular lymph spaces. The bile thrombi are interpreted as a manifestation of biliary inspissation, perhaps related to coagulation of a pathological albuminous exudate; but the basic cause is believed to be marked hemolysis in consequence of which the reticulo-endothelial system produces larger amounts of bilirubin.

Examined in the light of van den Bergh's test, later work has shown that we cannot classify all form of icterus as obstructive, whether of the large bile ducts or of the bile capillaries, as Eppinger's views on biliary thrombi (1908) led us to believe.

Newer Conceptions of the Pathogenesis of Jaundice.—For years a difference of opinion existed as to whether a true hemolytic (hematogenous)

[1] *Ergebnisse der inneren Medizin und Kinderheilkunde*, 1908, **1**, 107 (literature).

jaundice could take place without the participation of the liver, and the predominant opinion followed Naunyn, Minkowski, Stadelmann and others that all jaundice is hepatogenous in the sense that bile pigment is formed only in the liver. Owing to the work of Mann, this view must be abandoned. His experiments have proved conclusively that bilirubin can be formed outside the liver. Although the Kupffer cells of the vascular sinusoids of the liver play a considerable part in the production of bile pigment or its synthesis from hemoglobin, the work of many investigators has shown that in the large sense pigment metabolism is due to the joint action of the cells making up the recticulo-endothelial system.[1] In addition to the Kupffer cells, this system includes endothelial cells within the spleen, and to a less extent within the bone-marrow, the bloodvessel walls and the lining of the serous cavities. That these latter sources of bile pigment exist seems to be proved by Mann's observations showing that pigmentary jaundice occurs after total extirpation of the liver in dogs. Van den Bergh's work has been important in directing our attention in jaundice to the blood serum, rather than to a mere consideration of bile pigment present in the urine or its absence in the feces. His test shows that a latent form of jaundice exists—a preicteroid state—with an increased amount of bilirubin in the blood. This condition of minimal hyperbilirubinemia as a prelude to clinical jaundice is analogous to the hyperglycemia which precedes glycosuria.

To interpret the underlying pathology and explain the differences between van den Bergh's prompt direct, delayed direct, biphasic, and indirect reactions to bilirubin in the serum, McNee has advanced an attractive theory of the mode of production of jaundice, warranting its classification into (*a*) obstructive hepatic jaundice; (*b*) toxic and infective hepatic jaundice and (*c*) hemolytic jaundice.

McNee[2] believes that in *obstructive jaundice*, bile pigment has been normally formed by the reticulo-endothelial system and taken up in normal fashion by the polygonal cells lining the bile capillaries, normally excreted into them but obstructed in its outflow somewhere within the duct system. Because of this blockage, bilirubin, together with other constituents of the bile, reënter the blood. In this form of jaundice, van den Bergh's test gives a prompt direct reaction only.

In *toxic or infective hepatic jaundice*, (*a*) the polygonal cells of the liver have been damaged, so that bilirubin normally formed is unable to enter or pass through them, and instead passes directly into the hepatic vein radicals and accumulates in the circulation; (*b*) in the event of excessive blood destruction more bilirubin is formed than can pass through even healthy polygonal cells, the excess being carried into the circulation by the hepatic vein; this really amounts to a hyperbilirubinemia; (*c*) where, in addition to damaged polygonal cells there is obstruction in the ducts due to cholangitis, a combination which McNee believes occurs quite frequently. In toxic and infective hepatic jaundice, van den Bergh's test gives the biphasic reaction and McNee's view explains the simul-

[1] Aschoff, L.: *Muench. Med. Wchnschr.*, 1922, **69**, 1352 and *Lectures on Pathology* (Hoeber), 1924, Chapter I.

[2] *Quart. Jour. Med.*, 1922–23, **16**, 390; *Brit. Med. Jour.*, 1924, ii, 495, and 1925, ii, 52.

taneous presence of both of van den Bergh's varieties of bilirubin in the serum. In *hemolytic jaundice*, as seen in the ictero-anemias (associated with splenomegaly, pernicious anemia, worm anemias, etc.) there is a hyperbilirubinemia due to excessive hemolysis and the polygonal cells are unable to excrete the excessive overproduction of bilirubin rapidly enough. In this form of jaundice, van den Bergh's test gives the delayed direct reaction, or so delayed as to appear negative, and determinable only by the indirect test. McNee believes that there may often be combinations of these varieties of clinical jaundice and that toxic jaundice, with varying degrees of damage to liver cells, may be combined with hemolysis as well as with obstruction in the bile ducts.

In *catarrhal jaundice* both the prompt direct and delayed direct reactions may occur at one time or another. Uniformity of opinion is growing that catarrhal jaundice, in many instances, represents a mixed form of hepatitis due to a disorder of function of liver cells, associated with obstruction due to cholangitis. This supports the contention of the French school which believes that catarrhal jaundice is due to a toxic degeneration of liver cells, set up by an intestinal infection, the toxins being bacterial in origin.

Icterus neonatorum develops in from two-thirds to three-fourths of newborn infants on the second or third day of life, and usually fades within a week or ten days. The cutaneous discoloration is slight, and is commonly unattended by symptoms. The urine is often of normal color, and usually does not contain soluble bile pigments, but may reveal biliary granules or crystals in desquamated renal epithelium. The nature of this form of jaundice is not well understood. It has been attributed to compression of the biliary capillaries by distended portal radicles; to catarrhal cholangitis (Virchow); and to biliary stasis in consequence of the diminutive size of the bile ducts and consequent obstruction (Kehrer and Cohnheim). Frank attributed it to absorption of bilirubin from the meconium. Perhaps the disorder is really due to hemolysis in the early days of life. If this be the true explanation, the pathogenesis is that of hemolytic jaundice, as is suggested by the delayed or absent van den Bergh reaction. This benign form of jaundice must be distinguished from a more severe and often fatal form that may also occur in the early days of life in consequence of congenital syphilis, septicopyemia, congenital obliteration of the bile ducts, etc.

Chronic splenomegalic hemolytic jaundice[1] is a type which has been described under many synonyms calling attention to its hereditary or familial character, though some cases seem to be purely acquired. In the true familial type the jaundice, which is not very marked, dates usually from birth, or is noticed first during adolescence and occurs in several members of a family, often through a number of generations. The jaundice persists throughout the life of the patient but causes practically no symptoms. As Chauffard expressed it, these patients are rather jaundiced than sick. The urine and stools are highly colored, the urine

[1] Consult Chauffard: *Semaine med.*, 1907, **27**, 25; 1908, **28**, 48; Tileston and Griffin, *Am. Jour. Med. Sci.*, 1910, **139**, 847; Thayer and Morris, *Johns Hopkins Hosp. Bull.*, 1911, **22**, 85; Pearce, Krumbhaar, and Frazier, "*The Spleen and Anemia*" (Lippincott), 1918.

containing urobilin, and there is no evidence of biliary obstruction, the jaundice apparently being due to an excess of biliary pigment resulting from hemolysis. The van den Bergh test invariably gives a delayed direct reaction. Chauffard pointed out that the red blood cells show an increased fragility when they are exposed to hypotonic solutions of sodium chloride. The spleen is almost invariably enlarged, at times to enormous size; although the liver is usually not enlarged, it may be considerably so. These patients have "bilious attacks" quite commonly, even after slight indiscretions in diet and evidences of chronic toxemia, with drowsiness, lack of concentration, mental depression, etc.; they may have gall-stones and pain in the region of the gall-bladder is common. There is moderate anemia.

In the so-called *acquired form* there is not the same clean-cut picture; the patients usually show a more intense anemia and the fragility of the red blood cells is wanting. Recovery may occur after prolonged administration of iron in the acquired forms, but apparently cannot be expected in the hereditary cases. Chauffard[1] has changed his views on the apparent absence of danger in the congenital cases and states that serious complications may arise, such as cholangitis and cholelithiasis.

Effects of Jaundice.—The phenomena attendant upon jaundice are due largely to the underlying causes of which the jaundice is a symptom. The symptoms, however, as they are related directly to the jaundice and not to the underlying cause, are due on the one hand to the presence of biliary derivatives in the blood, and, on the other hand, to the absence of bile from the intestine. All the tissues and organs, with the exception of the nervous, are stained with biliary pigments; and in some severe cases of toxic or infectious jaundice the nervous system also may be stained. The staining is due, in part, to the deposition of biliary pigments in the tissues, in part to the circulation of blood and lymph containing pigments; it is most marked in the skin, mucous membranes, serous membranes, the liver, kidneys, heart, exudates, etc.

Mucous Membranes and the Skin.—Visible jaundice is manifested first by a yellowish discoloration of the conjunctivæ; in mild cases the discoloration is demonstrable there only. In the other visible mucous membranes, except that of the hard palate, the jaundice, unless of high grade, becomes apparent only after the tissues, by pressure, have been deprived of blood; the mucosa of the hard palate, however, being normally pale may reveal the discoloration without this.

The skin becomes of a characteristic lemon-yellow, orange-yellow, greenish-yellow, olive, or olive-bronze color. The discoloration is light in many cases of toxic or hemolytic jaundice, in which it is rarely more than moderate; it is light also in mild cases of catarrhal cholangitis; it is darkest in cases of permanent and complete obstruction of the common bile duct, and it may become so dark—olive bronze or greenish-black—as to warrant the designation black jaundice. The intensity of the jaundice in these cases is proportionate to the completeness of the obstruction of the common duct, or, in case the obstruction involves one of the larger

[1] *Bull. med.*, Par., 1912, **26**, 1159.

intrahepatic ducts, to the size of the duct implicated. The jaundice occurs earliest (sometimes within several hours) in cases of obstruction to the finer biliary ducts and capillaries, on account of the seat of the obstruction; it is delayed, commonly four or five days, in obstruction of the common duct, because the bile accumulating gradually distends the larger ducts and the gall-bladder. Time is required to produce sufficient pressure in the biliary canaliculi to cause their rupture into the adjacent lymphatic spaces and consequent absorption of bile. The pigment for the most part is deposited in the cells of the rete Malpighii, where in great measure it persists, often causing an obvious discoloration until the cells have been desquamated. It is for this reason that the cutaneous discoloration commonly persists a week, perhaps several weeks, after bile pigments have disappeared from the urine. Rous and McMaster, in their experiments on dogs and monkeys, have shown that they can tie off three-quarters or even five-sixths of all excretory ducts of the liver before clinical jaundice will appear, and often several days will elapse before its appearance; so great is the margin of reserve or compensating factor of the liver.

Of other cutaneous manifestations, *pruritus* is the most common and distressing. Rarely it precedes the discoloration of the skin; it is likely to develop in cases of jaundice of sudden onset; as a rule it is most marked in protracted severe cases; but it bears no definite relationship to the duration or the severity of the jaundice. The bile acids, absorbed into the blood, are thought to be responsible for the itching. Urticaria, perhaps due to a toxemia, is not uncommon. Considerable sweating, often localized to the palms, etc., is sometimes observed. Local infections, such as boils occasionally occur. In chronic cases, local *telangiectasis* of the skin (sometimes also of the oral and other mucous membranes) tend to develop, and flat or nodular yellowish, chamois-leather-colored patches (xanthelasma, xanthoma, vitiligoidea[1]) may appear on the skin or mucous membranes. These are most common in the skin of the eyelids, and in the folds and creases of the joints; they tend to be symmetrical in distribution; they have been observed on the gums, in the mucosa of the biliary ducts (perhaps in part answerable for the jaundice), etc. They are believed to be inflammatory or endothelial in origin, and to be due to the jaundice or an associated toxemia.

Blood.—Bile pigments are present in excess in the circulating blood, but whether they exert any deleterious effect on the blood itself has not been determined. The major toxic action of the bile is due to the bile acids—salts of glycocholic and taurocholic acids. Chauffard[2] calls attention to variations in the symptoms depending upon the predominance of one or other of the three principal elements of the bile (bilirubin, the bile acid salts of glycocholic and taurocholic acids, and cholesterin). Glycocoll and taurin result from hydrolysis of protein; the source of cholic acid is not definitely known. At the inception of jaundice these acid salts may be found in the circulating blood, but after jaundice is well established they usually disappear from the blood, being apparently

[1] Consult Futcher: *Am. Jour. Med. Sci.*, 1905, **130**, 939.
[2] *Presse med.*, 1913, **21**, 81.

produced in lessened amount, although the bile pigments continue to be produced in normal or almost normal amount. In ordinary obstructive jaundice the amount of bile acids in the blood is not sufficient to produce any noteworthy hemolysis; indeed, polycythemia is not uncommon. In toxic or infectious jaundice, hemolysis is common; usually it is itself the direct cause of the jaundice, but it may be increased by circulating bile acids. The *coagulation time* of the blood is much increased in jaundice —from the normal three to four minutes to ten to twelve minutes, or longer, a fact of much importance when surgical operations in jaundiced patients are under consideration. In protracted and severe cases there is a marked tendency to subcutaneous, submucous, and subserous hemorrhages.

Heart and Bloodvessels.—Bradycardia is a characteristic feature of jaundice, especially of acute cases and those of short duration. The pulse-rate may fall to 60, to 40, even to 21 (Frerichs) a minute, and it is subject to sudden fluctuations upon slight provocation. This has been attributed to a local inhibitory action of the bile acids on the cardiac muscle or ganglia; but perhaps the action is on the central nervous system. In chronic cases the bile acids become much reduced in amount or disappear, or the cardiac muscle becomes accustomed to their influence, and the bradycardia usually lessens or disappears.

Urine and Other Excretions.—In jaundice a considerable portion of the biliary derivatives is excreted in the urine, which is yellowish, yellowish-red, greenish, or greenish-brown, depending upon the relative amounts of bilirubin, biliverdin (its oxidation product), or urobilin (its reduction product). These bile pigments may be found in the urine several hours, or even several days, before there is any obvious discoloration of the skin. The urine often contains a number of hyaline, sometimes bile-stained, casts, attributable to irritation of the tubules provoked by excreting the bile pigments (which are not excreted by the glomeruli).

Urobilinuria[1] is common in disease of the liver. Urobilin, as well as urobilinogen, is formed in the intestine by the action of bacteria on bilirubin; they are absorbed and carried to the liver by the portal circulation. The occurrence of urobilinuria in cases of jaundice does not justify the designation "urobilin jaundice," since the cutaneous pigmentation is due to bilirubin and biliverdin.

Excretions other than urine also are stained in jaundice, such as the sweat (staining of the personal and bed linen), serous exudates and transudates, etc. The saliva, tears, mucus, and milk are not stained, unless a pathological inflammatory exudate be added to them. The sputum of complicating croupous pneumonia is stained, but not that of bronchitis.

The Liver.—Until recently, comparatively little has been known of the effect of jaundice on the liver, except in those cases in which biliary fistulas have been made. The opinion has been held that during the persistence of biliary obstruction bile is formed in lessened amount (oligocholia, hypocholia). In some cases, bile pigments seem to be formed in normal amounts, in others in lessened amount. French authors have

[1] Consult Hildebrant: *Ztschr. f. klin. Med.*, 1906, **59**, 351 and Wilbur and Addis, *Arch. Int. Med.*, 1914, **13**, 235 (literature).

described a colorless bile, said to contain bile acids and cholesterin, obtained from human beings with extreme fatty degeneration of the liver, as well as after duct obstruction (the "white bile" noted by surgeons). Rous and McMaster[1] by their experiments on dogs have done much to clear up the origin and causation of "white bile." Their findings "warrant the suggestion that the fluid is derived from the duct walls, while the liver cells have practically ceased secreting. However, this may be, there is no doubt that the ducts are the source of 'white bile' in obstructive instances." They further state that "the gall-bladder and ducts exert opposite influences upon the bile. The ducts fail to concentrate and thicken it with mucus as the bladder does, but dilute it slightly with a thin secretion of their own that is colorless and devoid of cholates even when the organism is heavily jaundiced. . . . . In obstructed ducts separated from the gall-bladder, or connecting with one so changed pathologically that the concentrating faculty has been lost, such fluid gradually replaces the small amount of bile originally pent up. When obstructed ducts connect with an approximately normal gall-bladder the stasis fluid is entirely different, owing to the bladder activity. At first there accumulates in quantity a true bile much inspissated by loss of fluid through the bladder wall, darkened by a change in the pigment, and progressively thickened with bladder mucus. As time passes duct secretion mingles with the tarry accumulation and very gradually replaces it. The inspissation of the bile, as indicated by the pigment content, is at its greatest after only a day or two of stasis. The differing influences of the ducts and bladder upon the bile must obviously have much to do with the site of origin of calculi and their clinical consequences." The use of the van den Bergh test has thrown additional light upon the effect of jaundice on the liver, as has also biliary tract drainage.

Nervous System.—Grave disturbances of the nervous system occur in many cases of jaundice; on the one hand, there are manifestations of depression, such as general neuromuscular weakness, asthenia, headache, vertigo, mental depression (that may progress to melancholia), insomnia, etc.; on the other hand, there are manifestations of irritation, such as severe headache, active delirium, coma, convulsions, etc. These manifestations are more common in acute toxic or infectious jaundice (associated with fever) than in the more protracted cases of obstructive jaundice; but they may supervene in any case of jaundice and not uncommonly lead to the fatal issue. They are commonly described under the name *cholemia*, but it is difficult to separate from one another the symptoms due to bile acidemia, to interference with the detoxifying function of the liver, and to the toxic or infectious process. The condition is not cholemia in a restricted sense, that is, it is not due to bile acidemia, since the symptoms may occur when bile acids are not in excess in the blood, as well as in cases of disease of the liver (such as cirrhosis) without jaundice. The condition is most likely an acid intoxication, due to disturbances of the detoxifying function of the liver, which may be brought about by disorganization of the hepatic parenchyma as in severe forms of toxic and

[1] *Jour. Exper. Med.*, 1921, **34**, 75.

infectious jaundice, acute yellow atrophy of the liver, phosphorus poisoning, starvation, diabetes, etc.

Gastro-intestinal Tract.—The absence of bile from the intestinal tract results, as a rule, in the passage of large, pale, grayish, slate-colored or clay-colored, pasty, fetid, acid stools. The pale color is due, in part only, to the absence of bile; in part it is due to the large amount of imperfectly digested fats, which may be increased from the normal 7 to 10 per cent. to as much as 80 per cent. Microscopically and chemically the fats consist of free fatty-acid crystals and soaps (calcium and magnesium) of the higher fatty acids; neutral fats are present in very small amounts. Rarely pale or decolorized stools contain biliary derivatives in considerable amount; this occurs especially in disease of the pancreas attended by obstruction to the outflow of the pancreatic juice but without jaundice. The pale color of the feces is due to the large amount of fat,[1] and to the reduction of bilirubin to leuko-urobilin.[2] It is not always warrantable to base on the color of the stools an opinion of the amount of bile that enters the intestine or of the degree of biliary stasis. The offensive odor of the stools is usually ascribed to the absence of bile which, when present, limits fermentation. Often, however, there is very little fermentation. Strasburger demonstrated no undue protein decomposition; and the odor may be described as peculiar rather than offensive, being due to the higher fatty acids. Constipation is perhaps the rule, and is due to defective motility, the result of lack of the stimulating influence of the bile. Sometimes the bowel movements are frequent, perhaps diarrhœic, which may be due to large fecal masses resulting from imperfect digestion of fat and to the laxative action of the free fatty acids. There is no effect on carbohydrate metabolism and very little on protein metabolism. If the acid secreting cells of the stomach are intact, gastric hyperacidity is more common, the biliary obstruction apparently causing an increase in the secretory activity of the stomach.

General Nutrition.—Man is able to withstand the effects of jaundice for a long time. The fatalities that ensue in the acute as well as in the chronic cases are due not so much to the jaundice *per se* as to other causes—the underlying cause of the jaundice, acid intoxication, etc. In long-standing cases, however, more or less disturbance of the general nutrition gradually ensues—due largely to imperfect fat absorption.

NON-SURGICAL DRAINAGE OF THE BILIARY TRACT[3]

This method, introduced in 1919, has been generally accepted as a practical procedure, both diagnostically and therapeutically. The method of non-surgical biliary tract drainage in its inception was based upon Meltzer's "law of contrary innervation" as applied to the biliary system, by using magnesium sulphate, peptone, olive oil, etc. as intraduodenal stimulants to bile discharge in general and gall-bladder emptying in par-

[1] Consult Gordon, Cammidge, Watkins, and Robson: *Lancet*, 1905, ii, 1687, 1803, 1951; 1906, i, 57, 185, 255.

[2] Schmidt und Strasburger: *Die Faeces des Menschen*, 1905, 2te Aufl. 225.

[3] For a full discussion of this subject the reader should consult the monograph of Lyon on "Non-surgical Drainage of the Gall Tract," Lea & Febiger, Philadelphia, 1923.—Editor.

ticular. As applied to the biliary tract, this law of Meltzer has been challenged because the experimental physiologists cannot demonstrate its validity or even agree in their findings. Sachs (U. S.), Pribram (Austria) and Matsuo (Japan) have visualized the gall-bladder expelling its contents as a result of intraduodenal stimulation with magnesium sulphate or peptone. Furthermore, there is now the proof of the gall-bladder emptying tetrabromphenolphthalein, or tetraiodophenolphthalein, using Graham's method of cholecystography, with intraduodenal magnesium sulphate stimulation, as shown by Silverman, Comstock and others.

The Present Conception of Gall-tract Disease.—Disease of the gall-tract is a manifold and composite one in which many organs are intimately, or remotely, involved. For many years, too great emphasis was laid upon the gall-bladder as the chief offender. Until recently we have not recognized clearly enough the infection and degenerative changes which take place in the liver, bile ducts, pancreas and intestines, which often play a prominent role in gall-tract disease and produce a widely varying digestive complex. To understand the protean nature of this disease, it is important to recognize not alone the close anatomical contacts between the stomach, duodenum, pancreas, liver, gall-bladder, ducts, and certain portions of the colon, but also to realize the interrelationship for producing or transplanting disease which exists between these organs because of their blood, lymph and nerve supply. The spleen, too, must be considered in connection with the portal system.

Difficulties in Diagnosis.—Acute intra-abdominal disease in no sense offers the diagnostic problems common to chronic gastro-intestinal disease. In acute disease, the intra-abdominal crisis often concerns predominantly one organ, whereas in chronic gastro-intestinal disease, there is rarely ever a distinct symptomatology involving one organ alone. A careful survey usually shows multiple interlocking disease or dysfunction of the mouth (its contents and accessory passages), stomach, duodenum, gall-tract, pancreas, appendix and intestines. Often disease, or disorder, of the nervous system, cardiovascular-splenic-renal systems or a disturbance in metabolism or endocrine glands, plays a part either as a contributing factor to, or sequel of chronic gastro-intestinal disease. Focal infection of tonsils, teeth, sinuses, lungs or bronchi, gall-bladder, appendix, colon, prostate and pelvic organs, and less frequently acute infectious disease often initiate such chronic disease.

The Present Therapeutic Status of Gall-tract Disease.—The real crux of the therapeutic problem lies in the proper selection (after thorough study) of patients in various stages of gall-tract and associated disease for whom appropriate surgical, non-surgical or combination methods are adapted. Many patients with gall-tract disease require and will recover good health from primary surgery alone, provided proper preoperative preparation has been given, good surgical technique exhibited, shock avoided and appropriate postoperative care is carried out. Others need never be operated upon and will recover health by non-surgical measures alone. Even with constant improvement in judgment and technique, there is still an undeniably high percentage of operative risk. After analyzing

23,723 gall-tract operations of all sorts, by American and Continental surgeons, the grand average mortality rate is 4.27 per cent. (Lyon). This analysis concerns series of cases of not less than 200 operated only by good surgeons. As a rule, the larger the series, the lower the mortality rate in unselected cases. Excluding the largest series of cases from one surgical clinic, a series of 6743 gall-tract operations from eleven good clinics (American and European) showed an average mortality-rate of 8.48 per cent. This is probably nearer the true mortality risk and certainly less than the figures would be if the operative statistics of less efficient surgeons were included.

Three Vicious Circles in Chronic Gall-tract Disease.—Recognizing the close interrelationship both anatomically and by reason of the lymphatic and vascular supply of the various organs draining into the portal system, and recognizing the better known functions of the liver and present status of functional tests the writer has attempted to show that there are three vicious circles concerned with the continued or relapsing ill-health of many chronically diseased gall-tract patients. At present this may be only theoretically assumed.

The first vicious circle is concerned with lymphatic drainage between the gall-bladder, liver and pancreas. If a bacterial cholecystitis exists, the gall-bladder becomes a focus of infection and the lymphatic distribution carries the infection to liver and pancreas and back again to the gall-bladder. Such gall-bladders are not relieved permanently by non-surgical drainage. The only way to break this vicious circle is to remove the gall-bladder. Occasionally the mural infection may die out or become attenuated after connective tissue overgrowth has become excessive but by this time the function of the gall-bladder has usually been destroyed and cholecystectomy is warranted. A common cause for such relapses lies in a preëxistent hepatitis which often creates a residual infection in the extrahepatic ducts and produces a relapsing cholangitis heretofore often requiring secondary surgery. In such cases, the liver, ducts and intestinal tract now become the chief focal point of infection and in them the second and third vicious circles become predominant. The liver or ducts, or more commonly both, continue to carry the infected bile to the duodenum. This disseminates the infection throughout the intestines until they in turn may develop mural as well as mucosal disease.

The *second vicious circle* consists in reabsorption of bacteria, or little known toxins in the bile, by the mesenteric veins emptying into the portal vein, thence back to and through the liver, part of the toxic dose being carried by the hepatic veins to the inferior vena cava but the larger part being reëxcreted by the liver to be again reabsorbed in the intestines.

The *third vicious circle* represents that toxic portion of the bile picked up by the mesenteric lacteals, emptied into the receptaculum chyli, and carried to the general circulation to exert a harmful effect on all tissues. Particularly important is the blood carried by the abdominal aorta to intra-abdominal viscera. After supplying the spleen, stomach, pancreas and intestines, the waste materials from such sources are in part carried again through their veins into the portal system and back to the overworked liver cells to be reëxcreted. As a result, the cardiac, renal and

blood-vascular, neural and intestinal systems exhibit a wide variety of symptoms. The liver possess a wide margin of reserve with great power of recuperation from injury but the continued absorption of toxins will injure the liver cells and impair or destroy their function and cause degenerative changes.

How can these second and third vicious circles be broken? Both are beyond the scope of surgery which cannot remove the liver or ducts. Non-surgical biliary drainage possesses great value because it removes from the body large quantities of bile containing bacteria and unknown toxic substances before they are absorbed. Experience has shown that by removing from the body by surgical drainage recoverable toxic factors in the bile the myocardial disturbance disappeared, the toxic irritation of the kidneys subsided and the digestive function improved during the period of drainage. Relapses occurred after drainage was terminated, presumably because the bile still contained infective or toxic factors. These evil effects of this can be controlled and often eradicated by non-surgical drainage in addition to other treatment.

The Development of the Method.—In 1917, Meltzer found that a solution of magnesium sulphate applied directly to the duodenal mucosa would relax the tonus of Oddi's sphincter of the common bile duct and cause an expulsion of bile into the duodenum. After experimenting with this salt on animals, Meltzer suggested that it might be clinically made use of by means of the duodenal tube. The writer developed this idea and established a system of biliary-tract drainage using as stimulants for bile discharge chiefly magnesium sulphate, peptone or olive oil. An hypothesis of so-called "A" "B" and "C" fractions of bile, representing bile from the ducts, gall-bladder and liver, was formulated. With the exception of the "C" or liver fraction (obtained in greatest purity), these biles are necessarily mixtures of the entire biliary system and represent in addition secretions from the pancreas, duodenum and stomach.

Its Value as a Diagnostic Procedure.—Briefly outlined, in inflammatory diseases of the gall-bladder and excretory ducts of the liver involving their mucous membranes, the microscopic findings disclose abnormal numbers of pus cells, exfoliated epithelial cells of different types, inflammatory mucus, crystal elements, bacteria, etc. Deviations from the gross appearance of normal bile, such as increased viscosities, turbidities, catarrhal flocculi, etc., can be observed. In cholelithiasis, the bile is microscopically often found loaded with crystals, more commonly cholesterin, calcium and bilirubin, up to macroscopic gall-stone sand. At times well-formed stones have been passed. Generally speaking, very dark black brown "B" fractions are more apt to occur in cholecystitis, whereas lighter shades, if pathological, are often obtained from gall-bladders containing stones. This may be due to a loss of concentrating power of a more severely damaged gall-bladder. The bacteria in colony formation, heavily bile-stained, culturally viable, when transplanted to rabbits and guinea-pigs, have been found (Kolmer) to be of pathogenic significance and very often show an elective affinity for the gall-bladder.

The dark colored "B" fraction is of gall-bladder origin in larger part. This bile uniformly secured from normal individuals is never recovered

in cholecystectomized cases *except* when the major excretory ducts are dilated or in conditions of chronic jaundice, or in various states of liver disease where there is biliary stasis in the smaller bile radicals within the liver or in cholecystectomies by high cystic duct ligation, or when bits of gall-bladder tissue are left behind.

In patients from whom no "B" fraction can be secured, the following diagnostic interpretations are suggested: (*i*) *Obstruction of the cystic duct* due to inflammation, swelling or congestion of the mucous membrane, inflammatory catarrh or choking of the duct with fine gall-sand or blocking by impacted gall-stones. (*ii*) Irritation of the racemose glands at the neck of the gall-bladder may produce a localized inflammatory œdema and block off the cystic duct. Bile can neither enter nor leave the gall-bladder. Here a hydropsical fluid is secreted by the racemose glands of the mucous membrane; the gall-bladder is often palpable but there is not clinical jaundice. (*iii*) Adhesions involving the cystic duct, stricture of the duct, angulation of the duct by pressure or otherwise (visceroptosis, pregnancy, tumor, enlarged lymphatic gland, impacted cystic duct stone, etc.). Jaundice never occurs from these causes alone, unless gland, tumor, or impacted stone blocks off the hepatic duct as well as the cystic duct. (*iv*) The gall-bladder may contain no bile if (*a*) its contents are multiple calculi, (*b*) if it is contracted around a single large stone or (*c*) if the gall-bladder is completely atrophic or fibrotic. None of these conditions in itself produces jaundice although it may be present from other causes. (*v*) The bile in the gall-bladder may be ultrastatic, tarry and too thick to flow readily or the gall-bladder musculature may be too weak to force it through the cystic duct. The above failures to obtain "B" bile are due to some form of mechanical block. (*vi*) There is likewise a "physiologic block" (Smithies) due to some defect in the neuromuscular mechanism of gall-bladder, ducts and sphincter which causes an uncoördinated response to normal neuromuscular reflexes (fatigue, local spasm, emotion, anger, fear, etc.). It has been noted in apprehensive Latin-Americans and in Hebrews.

Cystic duct obstruction due to *catarrh* gives an abnormal drainage sequence and a characteristic microscopic picture. Either no "B" bile is recovered, or only in small amounts, usually *preceded* by discharge of characteristic flocculi of dense yellow-brown mucus in shaggy, slimy masses. Microscopically, this mucus is unusually dense, often spiralled and encrusted with bile salts, etc., and, most important, an oleaginous material, possibly a fatty ester, pale to bright yellow, which melts out into globules, pools and lakes. In the above groups of cases, confirmation of cystic duct obstruction can usually be obtained by the Graham cholecystogram method.

In cholecystitis without cystic duct obstruction and in cholangitis, the biles are usually of abnormal color and increased viscosity, and microscopically show the reactions to inflammation in increased cellular exfoliation of bile-stained tall or short columnar epithelium, pus cells, bacteria, etc.

Non-surgical drainage when properly performed, can diagnose with accuracy (1) common duct obstruction, partial or complete, and often

differentiate its nature, (2) obstruction of the major pancreatic duct and (3) cystic duct obstruction, partial or complete, and often differentiate its nature. This method, therefore, offers the surgeon (1) advantages of a more accurate preoperative diagnosis—a better fore-knowledge of what he should find at the operating table, (2) a better selection of cases for which surgery is indicated, (3) if surgery is contraindicated, this method may be temporarily used as an alternative plan of treatment and in any event tends to lessen the surgical risk, and (4) the selection of patients who may postoperatively be protected against surgical failure by continuation of drainage by this method.

The *limitations* of non-surgical drainage are obvious. It cannot remove the gall-bladder of a focus of infection and thus break one vicious circle in the lymphatic drainage between infected liver or pancreas; it cannot safely or adequately remove gall-stones; or release obstructive adhesions or remove cancerous or gangrenous tissue.

Its Value as a Therapeutic Procedure.—There are two methods—the *intermittent drainage plan* and the *continuous drainage plan.* In the intermittent plan, a four- to eight-hour daytime drainage is given daily, semi-weekly or weekly, according to the original technique. A four-hour morning drainage will recover, on an average, 300 cc. of mixed bile of which three-quarters approximately will be "AC" fraction. An eight-hour day drainage will average about 600 cc. of which five-sixths represents "AC" fraction. If such drainages are carried out once a week for two months, the amount of bile recovered will average 2400 cc. or 4800 cc. removed from the body during that time. This amount is often sufficient to clear up the mildly catarrhal or infected gall-tract systems, but is not adequate in securing permanent improvement in the more severe grades of disease. Each drainage removes from the body much inflammatory débris and many bacteria. The transduodenal lavage with Ringer's or Jutte's solution flushes out the intestinal tract but despite eight weekly drainages, the catarrhal gall tract fills up for fifty-two out of sixty days. Therefore, in the more severe cases, the treatment must be intensified and the continuous drainage method used. Such drainage will recover and remove from the body an average of $3\frac{1}{2}$ to 4 gallons of bile in three weeks' treatment. This thoroughly drains the liver, aids its cells to function, flushes the ducts, prevents clogging with mucus, inflammatory or infected débris, avoids secondary stasis and minimizes the possibility of secondary calculi. It likewise drains the pancreas and lessens injury to the duodenal mucosa.

The *continuous drainage schedule* is as follows:

8.00 A.M.	Prepare mouth and stomach by thorough gargling and lavage.
8.30 to 12.00 M.	Duodenal drainage, stimulating with magnesium sulphate, peptone, olive oil, dilute hydrochloric acid, normal salt solution, or hot water (depending upon whether the gall-bladder has been removed or upon the individual drainage response to any of these solutions).
12.00 NOON.	The tube is then passed to a point 95 cm. from the teeth and the following duodenal feeding given:

		Calories
Milk (whole) . .	120 cc. (4 oz.)	80
Cream	15 cc. (½ oz.)	30
Yolk	1 egg	50
Lactose	15 gm. (½ oz.)	60
Salt	1 pinch	
		220

Predigest for ten minutes with peptonizing powder, put in thermos bottle at 105° F. and introduce slowly taking not less than thirty minutes for its introduction. If nausea, omit the egg-yolk, slow the rate of inflow, or both. Clamp off tube for additional half hour to permit this feeding to pass into the jejunum.

1.00 to 4.00 P.M. Draw up tube to 75 cm., mark and drain.

4.00 to 5.00 P.M. Repeat duodenal feeding.

5.00 to 8.00 P.M. Resume bile drainage.

8.00 to 9.00 P.M. Duodenal feeding.

9.00 P.M. Pull tube up to 75 cm. mark, unclamp and drain bile into gallon bottle throughout the night.

8.00 to 12.00 M. The following day, stimulate as before. Continue biliary drainage until noon. Give transduodenal lavaging enema of 250 cc. of Ringer's solution, or substitute suitable disinfectant—neutral acriflavine, mercurochrome, etc. *Remove tube.*

12.30 P.M. A lunch of cereal, soft egg toast, fruit juices or fruit.

3.00 P.M. Milk and crackers.

6.30 P.M. Dinner tray, either well balanced, or low in animal protein and fat and high in carbohydrate, sugar, starch, as indicated by knowledge of patient's gastric, duodenal, pancreatic and blood chemistry.

9.30 P.M. Milk and crackers.

That night the patient sleeps without the tube, and the following morning the foregoing schedule is repeated and so on over a period of two to four weeks, until 3 to 6 gallons of bile mixture have been recovered, *provided* the microscopic and cultural evidence parallels clinical improvement.

During this period of intensive treatment, the patient should be suitably controlled by additional studies (blood counts, blood chemistry, urinalysis, urine output, etc.).

Seclection of Cases for Treatment.—Biliary tract drainage, properly carried out, has great therapeutic value in the following groups:

1. *Relapsing cholangitis* (particularly after a cholecystectomy has failed to relieve) can often be cured without resorting to secondary operations, provided there is no evidence of a stone in common or hepatic ducts.

2. *Obstructive jaundice* due to impacted or ball-valve common duct stones. In many cases, the above plan aided by morphine, has lessened inflammatory œdema and sphincter spasm and permitted the stone to pass back into the dilated common duct. Occasionally, it has been passed and recovered in the stool. After drainage has been established, the jaundice rapidly clears, toxic myocarditis, nephritis and hepatitis subside, and surgery is safe at an earlier period.

3. When proper judgment is used in the selection of patients, many patients with *quiescent cholelithiasis* may be restored to satisfactory

health. Some cases of cholelithiasis with an inflamed mucous membrane of the gall-bladder and ducts may be relieved of colic and brought to a state of quiescence so that necessary surgery can be carried out at the most suitable period.

4. In many cases of gall-tract disease, including quiescent cholelithiasis, in which for some reason surgery cannot be undertaken, non-surgical drainage can be substituted with satisfactory results. When there are serious contraindications in gall-bladder disease requiring cholecystectomy, a week or two weeks of preoperative drainage improves the patient's condition and permits earlier surgery with increased safety.

5. Postoperative persistent hiccough and vomiting may be checked sometimes after the first few hours of drainage, certainly after a day or two. A number of cases of epidemic hiccough have been promptly aborted. In most of these cases, a streptococcus has been isolated from the bile. Postoperative adynamic ileus has been successfully treated by biliary drainage and duodenal lavage.

6. Some persistent *biliary fistulas* have been successfully closed by this form of drainage with the aid of vaccines.

7. Simple *catarrhal jaundice* usually clears promptly in from two to seven days after the obstructive plugs of mucus are removed. This spares the liver and pancreatic cells many days of pressure damage. Jaundice following arsphenamine treatment can be aborted and the function of the liver improved.

8. Early gall-bladder and duct catarrhs, with latent or unsuspected infection, diagnosable only by medical drainage study, can often be permanently cleared and more serious injury prevented. The objective drainage findings in many infectious fevers give evidence of the early mucosal damage to gall-bladder and ducts.

9. This continuous method of drainage is an excellent plan of treatment for gall-tract disease associated with duodenitis or the medical form of duodenal ulcer.

10. There is a large group of patients with hepatic-intestinal toxemia who give vague histories of atypical digestive symptoms, "biliousness," anorexia, constipation, headache, nausea, belching, etc., suggesting biliary or portal cirrhosis, but no definite evidence of gall-bladder or appendix disease. In many patients of this group, the gall-bladder and appendix have been removed. Medical biliary drainage and colonic irrigation often give excellent results.

11. In another group, severe sick headaches, suggesting biliary migraine, occur. Many such patients can be completely relieved.

12. Certain forms of *asthma* which do not respond to allergy tests seem to be due to some toxic factor within the gastro-intestinal tract and respond favorably to this treatment.

13. In association with other measures, some cases of chronic neuritis and arthritis have been greatly improved, particularly such joint cases as have infection within the liver or bowel. All recognizable extra-abdominal foci should be removed, if possible.

14. In a group embracing typhoid carriers, flagellate or other parasitic infections involving the biliary tract and upper intestines, this treatment

will be found helpful. Giardiasis is especially stubborn, and in its tendency to relapse *suggests* invasion of the gall-bladder.

15. There is a group embracing various diseases in some of which distinct improvement has been secured. In cirrhosis of the liver, when detected in an early stage, often accidentally at an operation, this treatment, when added to the orthodox management, offers some promise of preventing the later aspects of this disease. Among other cases benefited, the literature contains references to hemolytic jaundice and splenomegaly; pernicious or grave secondary anemia; chronic pancreatitis; diabetes; purpura hæmorrhagica; erythema nodosum; a non-traumatic form of epilepsy; biliary stasis with acute or chronic heart disease; intestinal stasis with attacks of mucous colitis associated with biliary and liver types of dyspepsia; hepatitis following lead, phosphorus or chloroform poisoning; acute yellow atrophy; and after operation on the biliary organs if derangement of hepatic function continues and further surgery is not possible.

Total Management in Gall-tract Disease.—This should embrace: (1) dietetic régime of frequent small feedings with reduced fat and animal protein content. The habit of skipping meals should be avoided. (2) Chemical therapy by mouth should be prescribed only to correct *known* disturbances of gastro-duodenal, pancreatic and biliary tract chemistry. (3) Vaccine therapy, preferably autogenous, in infections (focal). (4) Colonic irrigations[1] when indicated but for short periods only, as their continued and injudicious use favors the redevelopment of constipation. (5) Efforts directed to restoration of the normal bowel function, breaking the "laxative habit—constipation, vicious circle." (6) Definite education of the patient to so adjust his life as to place the least strain upon damaged organs (as in diabetes, tuberculosis, etc.).

Results Obtained.—In a study of 376 cases of biliary-tract disease reported by the writer,[2] 318 were treated by non-surgical measures alone, in which duodenal drainage was important. Some had incipient disease; some late disease with complications, and many were seriously ill. Thirty per cent. remained "cured" (*i. e.*, symptom-free for one to four years with normal objective findings); 52 per cent. were so much improved as to resume their occupations, discard further active treatment and remain in good health for longer than one year; 9 per cent., in a group representing illness of many years' duration, were considerably improved; 2 per cent. were entirely unimproved and only 1 patient (0.2 per cent.) died. Of this series of 376 cases, 52 had had previous gall-tract surgery without relief (an average of two abdominal operations per patient) and were badly incapacitated. This result was partly due to persistent postoperative complications, partly to a bad choice of the original operation, or incomplete exploration and consequent failure to recognize multiple lesions. Many had residual foci in the tonsils, teeth, etc., which partially accounted for relapses or unfavorable end-results. Of 52 cases, 27 were treated entirely by non-surgical procedures, including biliary tract drainage and vaccines, with marked improvement; 19 required further gall-

[1] See Norman: *Am. Jour. Electrother. and Radiology.* 1924, **42**, 116.
[2] *Therapeutic Gazette*, November, 1924.

tract surgery, preceded and followed by non-surgical drainage before health was restored.

The maximum drainage of the liver and ducts can be secured by the duodenal tube. The amount of bile drainage recovered by surgical intubation of common or hepatic ducts shows an average of less than 500 cc. in twenty-four hours (excepting in jaundice cases due to common duct obstruction), whereas an average of 1500 cc. bile drainage in twenty-four hours can be secured by the duodenal tube. All cases of advanced gall-tract disease *theoretically* require surgery, but cholecystectomy removes only one end-product of gall-tract disease and not the disease itself. *Practically* surgery might better be confined to removal of diseased structures (gall-bladder, stones, cancer, adhesions, strictures, etc.) or to short circuiting operations for non-removable obstructive lesions. To establish drainage later in non-obstructive lesions by duodenal tube methods offers a better chance of breaking the second and third vicious circles in chronic gall-tract disease.

ANOMALIES OF FORM AND POSITION

Congenital Anomalies of Form.—The liver is occasionally found in the thoracic cavity or projecting beneath the skin near the umbilicus (hepatomphalos); in monsters the organ may be entirely absent. Small portions of aberrant hepatic tissue are occasionally found in the suspensory ligament or the adjacent connective tissue. In partial and complete transposition of the viscera the liver may be as much in the left half of the body as normally it is in the right; in this event the left lobe is the larger. Rarely the normal relative size of the different lobes is changed; the left lobe may be unusually large or unusually small (defective blood supply during intra-uterine or early extra-uterine life); the smaller lobes may be smaller or larger than normally, and they are sometimes more or less pedunculated. Congenital linguiform lobulation of the right lobe has been described; it is commoner in children, and may be mistaken for acquired linguiform lobulation. Well-marked lobulation of the entire organ is occasionally encountered; sometimes, doubtless, it is a fetal manifestation; often it is a postnatal acquired condition due to syphilis, perhaps tuberculosis, perihepatitis, etc.

Acquired Anomalies (Deformities).—The important acquired deformities are: (1) The so-called corset, or constricted, liver; (2) linguiform lobulation; and (3) changes due to diseases of adjacent organs.

The corset, or constricted, liver is the consequence of tight lacing, and is therefore almost wholly confined to the female sex (as much as 25 per cent. of female cadavers in earlier series, now less common, due to changes in the customs in dress); but an analogous condition is sometimes encountered in men, the result of the constriction of a tight belt. The basis of the deformity is a pressure atrophy of the liver parenchyma followed by fibrosis. Sometimes there is only a deep circumferential furrow; usually the liver is considerably elongated and markedly thinned at the point of greatest constriction (most marked atrophy). In some cases but little hepatic parenchyma remains at the point of maximum constriction, and

the elongated portion of the right lobe, which may reach to the transverse umbilical line, is attached to the major portion of the organ by a fibrous hinge-like band. Various grades of this condition are encountered, and it gradually merges into that spoken of as a linguiform (or Riedel's) lobe. Occasionally the left lobe is similarly constricted and elongated. The surface of the superior part of the right lobe usually exhibits indentations corresponding with the ribs; occasionally the posterior margin of the left lobe is much infolded (corresponding folds of the diaphragm are usually encountered). The capsule of the liver and the overlying peritoneum are often much thickened, especially at the point of greatest pressure and constriction.

Linguiform lobulation is in many respects an exaggeration of the condition previously described. Both are common in female subjects, but the linguiform lobe, as pointed out by Riedel is intimately related to cholelithiasis and cholecystitis, enlargement of the gall-bladder being found in 60 per cent. of the cases. Tight lacing, however, is often at least partly responsible for the condition, since it doubtless leads to kinking of the cystic duct and consequent obstruction to the free flow of bile. These linguiform lobes are often long and much attentuated; and they are often extremely mobile. In consequence of long-continued congestion they may show the lesions of well-marked nutmeg liver with increase in fibrous tissue. They are comparatively commonly the seat of other diseases, such as gumma, abscess, tumor, etc.

Symptoms.—The corset liver and linguiform lobe may be entirely symptomless. In some cases there are symptoms of indigestion, as likely due to the tight lacing as to the changes in the liver. A lingual lobe is sometimes painful and tender, due to congestion or associated cholecystitis and cholelithiasis; occasionally nausea and vomiting ensue, and have been attributed to interference with the functions of the pylorus and duodenum; occasionally pains of biliary colic occur. In other cases the abnormality may be mistaken for an abdominal tumor.

Diagnosis.—This is not specially difficult when the conditions are borne in mind and the abdomen is examined carefully. Usually the abnormal lobe will be found to move with the liver during respiration, and it can be proved to be continuous with the liver, even when a coil of intestine courses over the most constricted part. The lobe may be mistaken for a dilated gall-bladder, floating kidney, hydronephrosis, tumor of the stomach, colon, pancreas, omentum, or ovary, appendicitis, etc.

Prognosis.—The prognosis depends upon the etiological factors and the advance made by the lesions.

Treatment.—The corset liver is better prevented than cured.

Acquired Anomalies of Position.—The liver may be displaced upward, downward, or laterally, or it may be rotated on its antero-posterior axis (anteverted or retroverted). Displacement downward results from disease above the diaphragm, such as pleuritis with exudation, hydrothorax, emphysema, tumor or abscess of the lungs or mediastinum, etc., as well as of subdiaphragmatic or suprahepatic abscess. Displacement upward results from disease of the abdominal organs, especially ascites, tympanites tumors, diaphragmatic hernia, etc. Frequently when displaced upward

the liver is also rotated posteriorly, so that the inferior surface presents anteriorly and upward, due to the liver being rather fixed posteriorly with the inferior vena cava. Occasionally the liver is tilted anteriorly, so that much of its upper surface comes in contact with the anterior abdominal wall; its anterior edge may fall as low as or lower than the umbilicus, whence enlargement of the organ may be simulated. This may occur in large aneurism of the descending thoracic or upper abdominal aorta, and in tumors of the kidney, adrenal, retroperitoneal glands, etc. The *symptoms* of such displacement of the liver are secondary to those due to the primary disorder. The *diagnosis* is usually obvious upon detecting the primary disorder; indeed, in some cases the evident displacement of the liver is a valuable aid in recognizing the primary disorder (pleural exudation, etc.). The displacement must be differentiated from other diseases, causing, on the one hand, lessening of the liver dulness and apparent diminution in the size of the liver (acute yellow atrophy, cirrhosis, intestinal distention, etc.), and those, on the other hand, causing enlargement of the liver (fatty and amyloid degeneration, cirrhosis, leukemic infiltration, carcinoma, sarcoma, etc.).

Hepatoptosis.—This is variously spoken of as hepatoptosis, wandering liver, movable liver, etc., a rare condition in which the liver is abnormally movable and presents variously in the abdominal cavity.

DISEASES OF THE HEPATIC ARTERY

Dilatation.—This occurs when the portal vein is obstructed (thrombosed or compressed), in which event the artery acts vicariously for the vein; this is seen especially when small branches of the portal vein are obstructed. The dilatation involves usually the branches of the hepatic artery, but it may extend to the main trunk. This compensatory action of the artery for the vein is never efficient. A compensatory enlargement of the hepatic artery is observed also in conditions of connective-tissue overgrowth, as in the advanced stage of cirrhosis. The capillaries especially are involved, but the process may extend to the main trunk. This is an important factor in causing the increased portal pressure and the consequent ascites in portal cirrhosis.

Thrombosis.—Thrombosis of the hepatic artery in man is such a rarity, not more than 2 cases (Ledien and Lancereaux) being on record, and 1 of these being doubtful, that its results are unknown.

Embolism.—Embolism of the hepatic artery is comparatively uncommon. Purely mechanical emboli are probably comparatively innocuous, on account of the free arterial anastomosis, and the part of the organ cut off from blood-supply by embolism of a small branch of the hepatic artery is doubtless supplied by blood from a collateral vessel. Embolism of the main trunk or principal branch has resulted in anemic infarction and necrosis. Infectious emboli are not rare; they occur in sepsis, involve the smaller branches of the artery, and give rise to multiple abscesses. Clinically the general condition usually overshadows the local lesions in the liver. Sarcomatous emboli are often observed in melanotic sarcoma, especially that originating in the eye.

Aneurism.—Aneurism of the hepatic artery is rare and in 1922, Friedenwald and Tannenbaum[1] collected 64 cases from the literature and report a case of their own making 65 in all. The disease is more common in males (4 to 1).

Pathology.—The aneurism may be extrahepatic or intrahepatic. Of the 65 cases collected by Friedenwald and Tannenbaum, 45 were extrahepatic, 18 intrahepatic, and 2 both extrahepatic and intrahepatic (two aneurisms in each). In 29 cases the main vessel was involved; in 23, the right branch; in 6 the left branch; and in 2, the cystic artery. The aneurism may be of the true or the false variety. Of the 65 cases, 45 resulted in rupture into the peritoneum, the biliary passages, the portal vein, the stomach, the duodenum, with associated rupture of the liver in the intrahepatic forms; 13 were found unruptured.

Symptoms.—The three most constant features are pain, jaundice, and hemorrhage. Pain is rarely absent; in typical cases it is paroxysmal and resembles that of biliary colic, being referred to the right hypochondrium and epigastrium, which are usually tender. Pain is usually absent between attacks. The pain is attributed to pressure on the hepatic plexus of nerves and to stretching of Glisson's capsule. Jaundice occurred in 27 of 49 cases in which there was a record. When present it is usually more or less permanent, and is due to pressure on the hepatic or the common bile duct. Hemorrhage occurred in 31 of 49 cases. Usually the blood reached the alimentary tract by way of the biliary ducts; rarely was there direct hemorrhage into the stomach or the duodenum; and rarely the bleeding was due to pressure on the portal vein and consequent passive congestion. Melena is the common clinical symptom; hematemesis is less common. The hemorrhage may be frequently repeated. Fever (as high as 104° F), occurred in a few cases, usually with the paroxysmal pain, and was sometimes accompanied by rigors. Disturbances of digestion are common, due to the effect of local pressure by the aneurism.

Diagnosis.—This is exceedingly difficult and in only 2 cases of the 65 was the diagnosis correctly made during life, except when operation was performed. Cholelithiasis, duodenal ulcer and pancreatic carcinoma are the diagnoses most commonly made. Hemorrhages are much less frequent in cholelithiasis than in aneurism of the hepatic artery; in aneurism hemorrhage may be the first symptom; in cholelithiasis, it is always late, usually due to fistula formation; the conditions may occur together. The association of symptoms of duodenal ulcer and of biliary colic might suggest the condition. The diagnosis becomes more positive if a pulsating tumor with a systolic murmur is evident in the region of the liver.

Treatment.—Should the condition be diagnosed, the hepatic artery or one of its branches should be ligated; a sufficient collateral circulation is likely to develop. All other treatment is palliative. Since the first successful operation performed by Kehr in 1903, 9 other patients have been operated upon and of these only 3 recovered.

[1] *Am. Jour. Med. Sci.*, 1923, **165**, 11 (literature).

DISEASES OF THE HEPATIC VEINS

Dilatation.—Dilatation of the hepatic veins and their branches is a concomitant of failure of the right side of the heart. The dilatation extends to the central vein of the hepatic lobule, and is often associated with thickening of the vessel wall, perivascular fibrosis, and pigmentation and atrophy of the surrounding hepatic parenchyma.

Thrombosis.—Thrombosis of the hepatic veins is a rare condition due to: (1) Intrahepatic or extrahepatic compression of the vein or its branches by a tumor, cyst, enlarged glands, etc.; (2) chronic stricture, the consequence of adhesions (perihepatitis) near the junction of the inferior vena cava; (3) neoplastic invasion of the vessel wall, which may progress to penetration of the vessel wall; (4) acute and chronic inflammatory disease of the vessel wall, syphilis, tuberculosis, etc., usually associated with interstitial hepatitis; (5) extension of a clot partially or completely occluding the inferior vena cava; and (6) occasionally it follows, sometimes precedes, thrombosis of the portal vein. The lesions are analogous to those of chronic passive congestion. Ascites and more or less enlargement of the spleen usually develop rapidly, but the condition is scarcely susceptible of clinical recognition. It may be suspected in cases of aggravated passive hyperemia upon the sudden onset of ascites.

Embolism.—Embolism of the hepatic veins is uncommon, and can result only from reversal of the blood stream.

Suppurative Phlebitis.—Suppurative phlebitis (thrombophlebitis) of the hepatic veins sometimes ensues in cases of acute infectious inflammation of the liver, suppurative cholangitis, hepatic abscess, etc., the infection being more prone to involve the hepatic veins than the branches of the portal vein, because the latter are comparatively well protected by a connective-tissue capsule. In the event of suppurative phlebitis of the hepatic veins, secondary abscesses in the lungs and general septicopyemia ensue.

Chronic Obliterating Endophlebitis.—Chronic obliterating endophlebitis of the hepatic veins, a disorder characterized by slow proliferation of the lining of the hepatic veins and consequent obstruction, is comparatively rare. Hess[1] in 1905 was able to collect only 23 cases, but believes that many cases have been overlooked, since clinically they resemble ordinary or portal cirrhosis of the liver, and unless at the necropsy the hepatic portion of the inferior vena cava is opened and the ostia of the hepatic veins examined, the clinical diagnosis of cirrhosis of the liver is likely to be declared correct. Nishikawa[2] has made an extensive study of this rare condition and collected 39 cases, 9 of which were his own. Of the 39 cases, 18 were males and 19 females; the sex of 2 cases was not recorded. The ages vary from thirteen to sixty-one, the average being thirty-one years.

DISEASES OF THE PORTAL VEIN

Thrombosis.—Thrombosis of the portal vein (pylethrombosis, pylephlebitis adhesiva) is more common in males than in females. It occurs

[1] *Am. Jour. Med. Sci.*, 1905, **130**, 986.
[2] *Mitteil. Med. Fak. der Kaiserlich. Univ. zu Tokyo*, 1918, **20**, 151–302 (literature).

at all ages, the average age in men being 44.8 years, and in women 41 years (Rolleston). The thrombosis may begin in the portal radicles within the liver, in the main trunk of the vein, or in the peripheral radicles anywhere within the area of collection of the vein; and subsequently by extension the process may become widespread.

Thrombosis of the intrahepatic radicles of the portal vein is the commonest form, and is due most frequently to cirrhosis. The cirrhotic process leads to gradual obstruction and ultimate isolation of certain sections of the portal distribution, and the increased pressure induces endophlebitis, in consequence of which the contained blood coagulates. The original coagula are gradually increased in size by secondary accretions, until not infrequently they become widespread, extending even to the main trunk of the portal vein. Thrombosis within the branches of the portal vein in the liver is also found in conditions that impede the local circulation, such as failure of the general circulation; inflammatory disorders; secondary new-growths, syphilis, etc.; in these conditions, however, the coagula, as a rule, are recent and of little clinical interest.

Thrombosis of the main trunk of the portal vein usually results from slow chronic inflammatory and degenerative processes in the wall of the vein (endophlebitis, phlebosclerosis, calcification), which in turn may be set up by a variety of processes. It may be a part of the cirrhotic process; it may be associated with chronic inflammatory process in its vicinity, that is, in the lesser omentum and peritoneum (thickening and induration, causing kinking and constriction of the vein), in the stomach and duodenum (ulcers with surrounding inflammatory induration), in the pancreas (swelling and induration compressing and distorting the vein); it may be due also to malignant and other new-growths of the stomach, intestine, pancreas, etc. The primary growth or the metastasis to regional lymph glands (hilum of the liver, retroperitoneum, mesentery, etc.), may implicate the main trunk or one of the larger branches that go to form it, and by compression, distortion, or invasion set up thrombosis. The thrombus may extend and become very extensive.

Thrombosis of the peripheral radicles that go to form the portal vein may be induced by inflammatory or neoplastic disease in any one of the organs of the gastro-intestinal tract, the spleen, the female genitalia, etc., that lead directly or indirectly to the portal vein. The primary coagula often increase in size until they reach the main trunk; or small portions may be detached and carried to the liver, causing embolism and more or less extensive secondary thrombosis.

The most frequent causes of thrombosis in any or all parts of the portal vein are cirrhosis of the liver and intra-abdominal new growths. Although commonly these thromboses do not undergo suppuration, bacteria not infrequently can be cultivated from them. This suggests that bacteria of attentuated virulence may be concerned in their formation, although one cannot exclude the possibility of secondary infection. It is not unlikely, however, that in at least some cases the bacteria set up a primary low-grade phlebitis, whereupon thrombosis follows.

Pathology.—The thrombus may be recent or old; not infrequently it is both: the one part pale, firm, fibrous, and intimately adherent to the

wall of the vein; the other reddish, soft and readily detached. It may completely or only partially occlude the lumen of the vein; or in the same case in one place it may completely and in another partially obstruct the lumen; that is, it may be annular, parietal, channelled, etc. The portal vein is usually thickened (phlebosclerosis); it not infrequently contains calcareous plates; and it may be represented by a firm, non-channelled fibrous cord (stricture or complete stenosis). Peripherally to the thrombus the portal vein is much dilated and tortuous, and a collateral circulation, analogous to that of cirrhosis of the liver, usually becomes established.[1] The liver presents the primary condition and sometimes, in addition, dilatation of the hepatic artery (compensatory), infarction, fatty degeneration, softening, necrosis, perhaps some fibrosis, etc. When there is thrombosis of the main trunk of the portal vein, or of the splenic vein, the spleen is enlarged and may show infarction. When the main trunk or the mesenteric veins are thrombosed, the small intestine shows hemorrhages and infarction, which may proceed to gangrene; this is usually most marked in the middle of the jejunum, which has no collateral circulation.

Symptoms.—Thrombosis of the portal vein may be entirely latent, that is, occurring usually in the course of other disorders; the manifestations of the primary condition usually entirely overshadow those due to the thrombosis. Sometimes, however, to the symptoms of the primary disorder others are added that may suggest the diagnosis. In about 60 per cent. of the cases (Langdon Brown)[2] the onset is acute; that is, although the thrombosis may be a gradual process, symptoms due to complete obstruction develop suddenly. The most marked consist of ascites, enlargement of the spleen, and various disorders of the gastro-intestinal tract. Ascites is present in 65.6 per cent. of the cases (Rolleston); it may be absent in cases that speedily terminate fatally, in those in which the mesenteric veins are involved chiefly or alone, and in certain cases of long standing in which an efficient collateral circulation has been established. As a rule the ascites develops rapidly, becomes extreme, and speedily reaccumulates after removal. The spleen is usually enlarged, often enormously engorged; but ascites and tympanites may prevent its ready recognition, and perisplenitis with adhesions may prevent enlargement. The spleen often decreases notably in size after gastro-intestinal hemorrhage. Of the gastro-intestinal symptoms, the most important are various dyspeptic symptoms, vomiting, hematemesis, and intestinal hemorrhage in 44.2 per cent. of cases (Rolleston), diarrhœa (serous or serosanguinolent, due to increased venous pressure), symptoms of intestinal obstruction (paralysis due to hemorrhagic infarction), hemorrhoids, etc. The abdomen may reveal dilated veins. The general condition is poor; the appetite, strength, and flesh fail; the urine lessens in amount (due to lowered blood-pressure); anemia, œdema, and finally cachexia supervene; and not infrequently phenomena of toxemia suggesting uremia appear, and the patient dies.

Diagnosis.—In most cases this is impossible, but it is suggested by the sudden onset of marked ascites, gastro-intestinal hemorrhage,

[1] Consult Pick: *Arch. f. path. Anat* (etc.), *Berl.* 1909, **197**, 490 (literature).

[2] *St. Barth. Hosp. Rep.*, 1901, **37**, 62.

enlargement of the spleen, abdominal pain, and symptoms of intestinal obstruction. When the intrahepatic branches or the main trunk of the portal vein are involved the disorder can scarcely be differentiated from cirrhosis, with which it is often associated; but a very acute onset suggests the thrombosis. Unusual enlargement of the spleen and copious hematemesis suggest involvement of the splenic vein; diarrhœa (serous or serosanguinolent) or abdominal pain, bloody stools, and symptoms of intestinal obstruction suggest involvement of the mesenteric veins.

Prognosis.—Many subjects die soon after the development of the thrombosis; the prognosis therefore is bad. In some cases, the process being gradual, a more or less efficient collateral circulation is established, which may prolong life for some time; in this event the duration depends largely upon the primary disorder, but it is rarely more than two years.

Treatment.—This is purely palliative, and resolves itself into that of serious hemorrhages and of ascites; the ascites usually requires repeated tapping. Operative intervention, to promote the formation of adhesions about the liver, or to remove the obstruction in the portal vein, is scarcely feasible. Splenectomy has been suggested.

Embolism.—Embolism of the intrahepatic branches of the portal vein is a rather common sequence of inflammatory, suppurative, ulcerative, and neoplastic processes of the organs within the area of collection of the portal vein. The most common antecedents of such embolism are appendicitis (with suppuration or ulceration and thrombosis of its veins), ulcerative processes of the intestine, notably dysentery, and tumors of the gastro-intestinal tract; but embolism occurs also in divers disorders in which thrombosis of the hemorrhoidal, mesenteric, gastric, or splenic veins develops. The emboli usually are small, and they are of significance largely on account of the conditions in the liver to which they may give rise, notably multiple liver abscesses, or secondary neoplastic deposits.

Suppurative Pylephlebitis.—Suppurative pylephlebitis (portal pyemia) is more common in males than in females; it is especially common in early adult life, coinciding with the age incidence of appendicitis. Like adhesive pylephlebitis, it may begin in the portal radicles within the liver, in the main trunk of the vein, or in the peripheral radicles anywhere within the area of collection of the vein; and subsequently by extension the process may become more or less widespread. Usually the process begins in the peripheral radicles, being secondary to ulcerative and suppurative processes of the gastro-intestinal tract. Of these the most common is ulcerative or suppurative appendicitis, more particularly in cases neglected surgically, or in which infectious thromboses occur in the appendicular and the mesenteric veins. Less commonly ulcerative and neoplastic processes of the stomach and intestines, such as gastric and duodenal ulcer, typhoid, tuberculous and dysenteric ulceration of the intestine, gastro-intestinal carcinoma, fissures, ulcer and strictures of the rectum and anus, suppurative or gangrenous pancreatitis, suppuration of the mesenteric glands, suppurative disease of the female genitalia, abscess of the spleen, etc., constitute the starting-point of the infective thrombosis. Occasionally, also, the process originates in operative infection of the mesenteric radicles of the portal vein (operations on the

intestine). The thrombus occasionally begins in the main trunk of the vein, sometimes in consequence of operative trauma, but usually secondarily to a local focus of suppuration—perigastric, periduodenal, subhepatic, etc.; or to gall-stones in the common duct, with surrounding suppuration, etc. Suppurative pylephlebitis rather rarely begins within the liver, but it may be sequential to a liver abscess, suppurating hydatid cyst, suppurative cholangitis (with or without cholelithiasis or cholecystitis), etc. In these cases the infection is much more likely to involve the hepatic rather than the portal vein, since the latter is protected by a connective-tissue envelope; but infection of the portal vein does occur, doubtless by the lymphatics, although sometimes by continuity.

Pathology.—The process may be more or less localized or quite widespread. Usually the peripheral radicles and some of the main branches of the vein are involved; sometimes the process involves also the main trunk and extends into the liver; in some cases the peripheral radicles and the ramifications in the liver are implicated, the main trunk being almost if not quite free; in this event the intrahepatic lesions are embolic. The vein is enlarged, swollen, softened, congested, œdematous (panphlebitis); it is filled with a more or less softened (necrotic) sanguinolent-purulent or purulent material partially or completely obstructing the lumen. When not entirely liquefied the clot is more or less friable, occasionally free in the lumen, but usually it is more or less intimately attached to the intima. Not infrequently there is obvious purulent infiltration of the wall of the vein, and a sheath of pus or purulent material about the vein (perivascular lymph spaces) and in the adjacent connective tissue, usually on the right side. The liver is usually enlarged and contains foci of necrosis or multiple abscesses; the spleen is enlarged and softened; not infrequently there is localized or generalized purulent peritonitis; there may be a purulent pleuritis; and sometimes secondary abscesses develop in different regions of the body.

Symptoms.—Since suppurative pylephlebitis is a secondary disorder, the symptoms directly attributable to it are preceded by those of the disease to which it owes its origin, notably appendicitis. The onset of the pylephlebitis is usually sudden, and is manifested by the phenomena of septicopyemia: irregular chills, fever, and sweats, a soft, compressible, rapid pulse, leukocytosis, and general prostration. To these may be added extension of the abdominal pain beyond the seat of original disease, enlargement and tenderness of the liver (about one-half of the cases), enlargement of the spleen (one-fourth of the cases), etc. Vomiting, hematemesis, and diarrhœa are sometimes observed. Symptoms referable to various complications (pleuritis, brain abscess, etc.) may supervene.

Diagnosis.—This rests upon an obvious primary cause, the development of a septicopyemic state, and evidences of involvement of the liver (enlargement, tenderness, and perhaps slight jaundice). In the differential diagnosis one has to consider other forms of liver abscess and of septicopyemia, typhoid fever, etc.

Prognosis.—The disorder is fatal in the great majority of cases, especially when the main trunk of the vein is involved or when there are multiple abscesses in the liver.

Treatment.—The disease is much easier prevented than cured. Appendicitis should be promptly treated surgically, and other ulcerative or suppurative conditions of the gastro-intestinal tract should be appropriately treated, so as to prevent the formation of infectious emboli. When developed the treatment is that of liver abscess.

Chronic Endophlebitis.—Chronic endophlebitis, a process allied to arteriosclerosis, apparently may be primary or secondary. The primary process is exceptionally rare, and its etiology is ill understood; doubtless some cases are due to syphilis; in splenic anemia, hyperplastic changes initiated in the endothelium of the blood-sinuses of the spleen may gradually spread to the splenic and the portal veins, and ultimately involve the portal radicles in the liver; to this is attributed the sequential cirrhosis of the liver. Secondary endophlebitis of the portal vein occurs in hepatic cirrhosis and advanced passive congestion. In these cases it is usually attributed to the increased pressure, but toxic products may play a part. Partial or complete thrombosis may follow chronic endophlebitis; and calcification is not uncommon.

RETROGRESSIVE DISORDERS OF THE LIVER

Atrophy of the Liver.—This is a term more or less generally but inaptly applied to conditions in which the liver becomes reduced in size. Most of these conditions are degenerative and not truly atrophic.

Localized atrophy occurs under most diverse circumstances, generally in consequence of pressure, such as tight lacing, or belts, deformities of the chest and vertebræ (kyphosis and scoliosis), tumors and other disorders of adjacent organs, etc.; it occurs also in certain diseases of the liver itself, such as in the vicinity of tumors and cysts, in consequence of the occlusion of a branch of the portal vein or hepatic artery, and in passive congestion, amyloid disease, cirrhosis, etc. Under these varying circumstances there is a more or less localized reduction in the size of the liver, which may be: (1) Truly atrophic with subsequent replacement fibrosis, as in pressure exerted by corsets or other constrictions, etc.; or (2) atrophic and degenerative (especially fatty degeneration and necrosis), as in passive congestion, amyloid disease, cirrhosis, etc.

General atrophy may follow stenosis or occlusion of the portal vein; general hepatitis with thickening of the capsule; advanced cirrhosis, advanced passive congestion, etc.; and a reduction in the size of the liver, which, however, is not a true atrophy, follows many widespread degenerative processes, such as acute yellow atrophy, and poisoning by phosphorus, arsenic, chloroform, etc. A decrease in the size of the liver, to which the term atrophy is truly applicable, occurs in general wasting, as in senile atrophy, inanition, etc. The liver becomes reduced in size, because of a reduction in size and possibly also in number of the liver cells, without degenerative changes in the hepatic parenchyma or noteworthy changes in the interstitial tissues. In senility the liver participates in the general atrophic process. Otherwise this general atrophy of the liver is due to disturbances of metabolism brought about by: (1)

Deficient nourishment; or (2) excessive waste due to malignant growths, protracted suppuration, etc.

Pathology.—The liver is reduced in size, dark in color, dense, flaccid, of increased specific gravity, and dry—changes attributable to disappearance of the parenchyma and relative increase of the connective tissue. The section surface is dry, and the acini are obviously reduced in size and perhaps in number. These changes, although widespread, are not uniform, the margins, as a rule, being relatively more affected than the central portion of the lobes. The liver cells are reduced in size and number, and often contain considerable pigment.

Symptoms.—The symptoms are those of the primary disorder.

Parenchymatous Degeneration.—This (cloudy swelling) is perhaps the commonest deviation from the normal exhibited by the liver. To some extent it is a physiological process and is seen when excessive demands are made upon the liver. Otherwise cloudy swelling results from the action of divers poisons, bacterial and non-bacterial. The process is especially common in the infectious diseases, notably typhoid fever, pneumonia and dysentery. The liver is enlarged, somewhat softened, of lessened elasticity, pale, somewhat dull and opaque (as though cooked), and on microscopic examination reveals swelling, increased granulation and opacity of the liver cells, and obscuration of the nuclei. The condition is of secondary clinical interest, being only a part of general toxemic processes. Clinically some enlargement and occasionally tenderness of the liver may be elicited.

Gaseous or Emphysematous Liver.—This is characterized by numerous gaseous cysts in the liver due to *Bacillus aërogenes capsulatus*. The infection is rarely primary, although the organism has been cultivated from the blood before death; usually it is secondary, and occurs at or about the agonal period or after death from other causes. The organism is usually found in association with other bacteria, and although present before death, the gas formation is a postmortem phenomenon. The liver is most commonly involved, but the process may be widespread. The infection usually occurs by way of the portal vein (from the intestinal tract); but it may occur by way of the general circulation, or directly from the intestine to the biliary ducts and the gall-bladder. The liver is enlarged, soft, and spongy, and is pervaded by numerous usually small gaseous cysts. The condition is chiefly of pathological interest, and is not susceptible of clinical recognition.

Fatty Liver.—This is a comprehensive term applicable to the different conditions characterized by an excess of fat in the liver. On the one hand it includes fatty infiltration, in which there is an excessive deposit of fat in otherwise unaltered or slightly altered liver cells; and on the other hand, fatty degeneration, in which in addition to the fat there are greater or less degenerative changes in the hepatic parenchyma, perhaps the direct conversion of the liver cells into fat. Formerly the two conditions were differentiated; doubtless there are extreme cases of fatty infiltration and of fatty degeneration, but many cases partake of the nature of both processes, and there is considerable evidence that the fat in the liver under all circumstances is derived mainly from adipose

tissue elsewhere in the body; that even in phosphorus poisoning the fat in the liver is not due, wholly at least, to conversion of the liver protein.[1] It seems impracticable, therefore, to differentiate fatty infiltration sharply from fatty degeneration; both processes are appropriately discussed as fatty liver, or fatty changes in the liver.

Etiology.—The causes are: (1) Dietetic indiscretions and associated disorders of metabolism, notably the ingestion of too much food, particularly fat and carbohydrates, to which is usually added a sedentary life and lack of exercise—factors that tend to produce obesity, of which fatty liver (mostly infiltration) is a conspicuous feature. The fatty deposit is ascribed to incomplete oxidation of the excessive amount of food. (2) Anemic and cachectic conditions, such as occur in the late stages of many chronic disorders, such as tuberculosis, carcinoma, etc., in which there is deficient oxidation; but the influence of toxic substances may not be ignored. (3) Passive congestion—in which the fatty infiltration of the periphery of the liver lobules is in marked contrast to the congested centres (nutmeg liver). (4) Poisons of most diverse nature, notably chronic alcoholism. Alcohol seems to a be definite protoplasmic poison to the liver cells, and in addition to taking oxygen for its own combustion, gives rise to deficient oxidation of other food products. The fatty changes are often associated with cirrhosis (fatty cirrhosis). Other poisons causing fatty changes are minerals, such as phosphorus, arsenic, mercury, etc.; mineral acids, such as hydrochloric, nitric, etc.; and other chemicals, such as chloroform, phloridzin, tetrachlorethane, trinitrotoluene; etc. (5) Certain local infections of the intestinal tract, such as the gastrointestinal catarrh of children, dysentery, etc., in which toxins are carried to the liver by the portal vein. (6) Certain general infections, notably streptococcic and staphylococcic and other pyogenic infections of long duration, tuberculosis, etc. The exact cause of the fatty liver that occurs in about one-third of the cases of tuberculosis is not well understood, although doubtless it is related to deficient oxidation.

Pathology.—Usually the liver is enlarged and may weigh 3000 to 4000 gm.; it is of lessened specific gravity (sometimes floating in water), and of lessened resistance; it is normal in conformation, and has a smooth surface and rounded edges, and is pale yellowish in color. The section surface is usually pale, anemic, obviously fatty; in cases of passive congestion the well-known appearances of nutmeg liver (dark centre and light periphery of the lobules) are seen; and in fatty cirrhosis the association of fibrosis is obvious. Histologically the cells at the periphery of the lobules contain fat droplets that vary much in size and displace the cellular protoplasm and nuclei, which otherwise are not notably altered; after removal of the fat the cells may revert to their normal condition. Fatty degeneration may involve any part of the liver lobule but is most often in the central zone;[2] the cells reveal minute droplets of fat throughout the protoplasm, which otherwise is markedly granular, distorted, and opaque; the nuclei, at first unaltered, soon undergo retro-

[1] Adami: *Principles of Pathology*, 1911, **2**, 430 and 905.
[2] McCrae and Klotz: *Jour. Exp. Med.*, 1910, **12**, 746.

grade change; after removal of the fat the cells are shrunken, opaque, and evidently the seat of retrograde metamorphosis.

Symptoms and Findings.—These are ill-defined and may be due to the initiating disease and the degenerative change in the liver cells rather than to the mere presence of fat. In general the symptoms are those of the primary disorder, obesity, tuberculosis, alcoholism, etc. In perhaps the majority of cases there are no symptoms referable directly to the liver; occasionally discomfort may be due to its weight, and ill-defined dyspeptic symptoms may be attributed to functional inactivity of the liver, although they are more likely to be due to associated disorders of the stomach and intestines, etc. The liver is enlarged and commonly palpable two or three finger-breadths below the costal margin; excessive fatty deposit in the abdominal wall, as well as the flaccidity of the liver itself, may render examination unsatisfactory. In thin tuberculous subjects the enlarged liver is usually readily palpable. In associated cirrhosis and amyloid disease, etc., the liver is usually firm and more readily palpable.

Diagnosis.—Minor grades of fatty liver cannot be recognized with certainty; the more marked grades must be differentiated from other causes of enlargement. The fatty cirrhotic liver occasions the symptoms of cirrhosis, notably hematemesis, ascites, and enlargement of the spleen, which do not belong to the fatty liver. The amyloid liver is much firmer than the fatty, has a more or less obvious cause, and is associated with amyloid disease elsewhere. Leukemic enlargement of the liver is readily recognized by the blood examination. The enlarged liver of passive congestion is readily determined by recognizing an obvious cause. A displaced liver should be recognized by a careful examination. The liver of phosphorus poisoning should be determined by the history, general phenomena, and the subsequent development of jaundice, which does not occur in other forms of fatty liver.

Prognosis.—The prognosis depends upon the primary cause.

Treatment.—The treatment is altogether that of the primary disorder, obesity, alcoholism, etc., of which, from a therapeutic point of view, the fatty liver usually constitutes an almost negligible associate.

Amyloid Degeneration.—This is a process characterized by the conversion of the proteins of the tissues into a structureless homogeneous substance called lardacein.

Etiology.—Amyloid degeneration is a disease of young male subjects (usually less than thirty years). In the majority of cases it follows prolonged suppuration, especially that due to syphilis and tuberculosis and involving the bones and the lungs. Less commonly it occurs in the absence of suppuration, as in the cachexia of tertiary syphilis, chronic malaria, malignant disease, and in delayed convalescence from infectious diseases. In most cases the direct cause seems to be the absorption of the toxic products of pyogenic cocci.

Pathology.—The relative frequency of involvement of the different organs is shown by the combined statistics of Birch-Hirschfeld, Loomis, Dickinson, Goodhart, and Turner. Of 795 cases the spleen was involved in 585, the kidneys in 539, and the liver in 387 (Rolleston). The amyloid

liver is enlarged, sometimes to four or five times its normal size; its general conformation is preserved, its edges are sharp or slightly rounded, and its surface smooth; it is pale in color, firmer than normal, of increased specific gravity and lessened elasticity. The section surface is smooth, pale, grayish red in color, and peculiarly translucent, glistening, or bacony in appearance (especially apparent at the edge of the cut surface). In minor grades the individual lobules are more or less obvious, but later they lose their identity. A fresh cut surface treated with iodine strikes a mahogany-brown color, which occurs in more or less ring forms in the mid-portion of the lobules, the remaining portions (centre and periphery) of the lobules being pale yellowish or yellowish brown. Microscopically, the amyloid material is first found in the subendothelial layer of the capillaries of the mid-zone of the liver lobules; later it involves other capillaries and arterioles and spreads to the media; still later similar changes occur in the small venules, and ultimately the process involves the adjacent connective tissue. On account of defective nutritive supply, and doubtless also in consequence of the direct action of toxins, the parenchymatous cells show cloudy swelling and fatty degeneration, and are ultimately removed or converted into amyloid material.

Symptoms and Findings.—The symptoms are those of amyloid disease in general—progressive emaciation, anemia, and debility, usually in a person the subject of chronic suppuration or syphilis. The liver is enlarged (it may reach much below the umbilicus), painless, smooth, firm, and has sharp or somewhat rounded edges. The spleen is usually enlarged and firm; often there are evidences of amyloid degeneration of the kidneys (polyuria, albuminuria, waxy casts, etc.), of the intestinal tract, (diarrhœa), and of the cardiovascular system (weak heart, low blood-pressure, œdema, etc.). There is no jaundice or evidence of portal obstruction, except in the event of complications.

Diagnosis.—This is comparatively easy in some cases: a history of syphilis, or of long-standing suppuration, with enlargement of the liver and spleen, albuminuria, and perhaps diarrhœa, or weak heart and œdema, is quite unmistakable. Amyloid must be distinguished from other painless enlargements of the liver. The fatty liver is usually associated with obesity, alcoholism, etc., and the liver is softer. The fatty cirrhotic liver is likely to be tender, there are the antecedents of cirrhosis and its more common phenomena. Leukemic enlargement is readily recognized by a blood examination.

Prognosis.—This is bad, although some improvement may be effected; occasionally the liver becomes considerably reduced in size.

Treatment.—The essential part is to eliminate the cause; suppurative foci must be adequately drained and the suppuration stopped as soon as possible; syphilis should be appropriately treated. Attention to the general health is of the greatest importance, and comprises good food, fresh air, rest, syrup of iron iodide, etc.

Pigmentation of the Liver.—This occurs under a variety of circumstances, but in itself is of comparatively little clinical importance. Certain extraneous pigments are sometimes found, such as coal-dust (anthracosis), stone-dust (silicosis), silver (after medicinal administra-

tion), etc. The associated changes are usually those of slight or moderate fibrosis, to which perhaps the extraneous pigmentation may be etiologically related. Of intrinsic pigmentation the most important are bile pigment and other derivatives of hemoglobin. Normally the liver cells usually show a varying number of fine yellowish-brown granules—some iron-containing (hemosiderin), some iron-free (hemofuscin); these are likely to be increased in atrophy of the liver cells from senility or other causes. Bile pigments (usually bilirubin, sometimes biliverdin) are found normally in the biliary passages; in cases of obstruction to the free flow of bile these pigments are found in excess in the biliary passages and also in the liver cells (particularly necrotic cells), and in the interstitial tissue. In malaria there occurs a deposit of fine dark-brown or brownish-black pigment granules, especially in the endothelial cells of the capillaries at the periphery of the lobules and in the perivascular connective tissue, and in the Kupffer cells which act as phagocytes; occasionally there is some associated fibrosis that has been described as a malarial cirrhosis. A deposit of iron-containing pigment (siderosis of the liver) is found in and about various local lesions (abscesses, gummas, scars, tumors, etc.), in chronic passive congestion, cirrhosis, pernicious anemia, leukemia, and hemochromatosis; and a special metabolic pigmentation is found in melanotic sarcoma. Sprunt, Colwell and Hagan[1] believe that iron-containing, as well as other kinds of pigments, may be formed during autolytic degeneration of parenchymatous cells independently of the hemoglobin in the blood. In the nutmeg liver of chronic passive congestion, iron-free and iron-containing pigment is found in and about the central veins; it becomes quite conspicuous in the advanced stages (red atrophy), in which a large section of the central part of the lobules may show such pigmentation; later the iron reaction may no longer be obtainable. In pernicious anemia the periphery of the liver lobules usually contains a considerable excess of iron-containing pigment, found also, but in less degree, in some cases of leukemia.

Hemochromatosis.—In this the liberated hemoglobin is deposited as pigment granules in the skin, liver, pancreas, etc., and gradually, fibrosis of the liver and pancreas occurs. Mallory[2] has pointed out that chronic poisoning with copper may be the cause of hemochromatosis. Although the well-developed disease is comparatively rare, the early lesions are fairly common but usually remain unrecognized. Mallory tabulates the sources of such poisoning as follows: (1) Distilled liquors contaminated with copper dissolved from the copper worm of the condenser by action of volatile organic acids (citric, acetic, etc.). (2) Occupations involving exposure to copper dust (brass foundries, brass milling, planing and polishing, telephone line repair) as the metal is readily dissolved in the juices of the body, however it may obtain entrance. (3) Probably acid foods, jellies, candies, etc., contaminated by copper owing to cooking in copper vessels. Under this last heading must be included foods cooked and fried in copper kettles and pans, owing to the dissolving action of oleic, palmitic and stearic acids in fats on the metal. Experimental work with

[1] *Jour. Exper. Med.*, 1912, **16**, 607.
[2] *Am. Jour. Path.*, 1925, **1**, 117.

animals demonstrated that copper inhaled or ingested is dangerous to life, although its action as a chronic poison is exceedingly slow. Mallory's studies indicate that it ordinarily takes fifteen to twenty-five or more years to produce well-developed hemochromatosis. The youngest case seen by him was aged thirty-one years; the great majority ranging from thirty-eight to sixty years in age.

Pathology.—In hemochromatosis, the yellow pigment, hemofuscin, derived from hemoglobin, is deposited in the endothelium lining the sinusoids, and in the parenchymatous cells of the liver. In the course of time it is changed to hemosiderin. After the liver cells have taken up as much pigment as they can hold, it then begins to be deposited in the other organs and tissues, especially in the pancreas, cortex of the adrenal glands, lymph nodes in the upper part of the abdomen, the heart, thyroid, skin of the extremities, mucosa of the stomach, etc. In the pancreas, necrosis, regeneration and sclerosis occur as in the liver; the result is to cause diabetes mellitus. Destruction of the cortex of the adrenal glands may lead to increase of the normal pigment (melanin) in the skin and other tissues, as in Addison's disease. Pigmentation of the heart may result in necrosis of muscle fibres and sclerosis.

Treatment.—The treatment is largely preventive. With the dangers of chronic copper poisoning, proper means should be taken to protect persons in industrial occupations such as those mentioned above, and special care should be given to the avoidance of use of copper-lined cooking receptacles, especially when such utensils are used in the preparation of fried foods.

Leukemic Infiltration.—The leukemic process commonly involves the liver: the lymphocytic variety always, the myelocytic variety almost always, although the disease may be quite advanced before noteworthy changes occur in the liver. The liver is enlarged, sometimes weighing 6000 gm. or more, that is, three or four times its normal size; its surface is smooth, its edge somewhat rounded, and it is of lessened resistance and density. The section surface is smooth, pale, opaque, grayish, or sometimes yellowish in color. The individual lobules are usually distinguishable, and may appear to be more widely separated than normally (periportal leukocytic infiltration). Occasionally small roundish masses (lymphomatous masses), suggesting miliary tubercles can be detected. Microscopically there is widespread leukocytic (lymphocytic or myelocytic) infiltration.

Symptoms and Findings.—The symptoms are those of leukemia, the enlargement of the liver being a part of the disease. The enlarged liver is painless, smooth, and has fairly sharp edges. Ascites, which is not rarely a terminal event in leukemia, has been variously interpreted. In many cases it is doubtless due to the blood dyscrasia and failing cardiovascular system; in some cases it may be due to peritonitis, sometimes tuberculous; it has also been attributed to obstruction or thrombosis of the portal radicles.

The *diagnosis* is made by an examination of the blood. The *treatment* is that of leukemia.

Necrosis.—This may occur as a widespread or a limited process. The widespread process, such as occurs in thrombosis of the hepatic artery or the portal vein, in acute yellow atrophy of the liver, tropical abscess, etc., is elsewhere discussed. The limited process, so-called focal necrosis (Mallory), occurs under a variety of circumstances and in several forms, which, however, are of pathological rather than clinical interest. Central, peripheral, and mid-zonal forms have been described; the underlying factors of the varying zonal distribution of the necroses have not been definitely determined. Most of these necroses are found in acute infections, such as typhoid fever, scarlet fever, diphtheria, pneumonia, cerebrospinal fever,[1] etc. In some cases, doubtless, they result from the direct action on the liver cells of bacterial toxins; in other cases they follow obstruction or occlusion of the capillaries by swollen, proliferated, or desquamated endothelial cells, transported giant (usually phagocytic) cells, fibrinoid plugs, thrombi made up of agglutinated erythrocytes, etc. Experimentally they may be induced by injection into lower animals of vegetable poisons, such as abrin and ricin (Flexner), or of hemagglutinins of bacterial origin or those contained in certain cytolytic immune sera (Pearce) which lead to the formation in the portal radicles of thrombi made up of agglutinated erythrocytes. These have a clinical interest in that they suggest the lesions as well as the mode of development of cirrhosis of the liver.

Oertel[2] has described a multiple non-inflammatory necrosis of the liver with jaundice, and he and Symmers[3] have carefully described the changes that occur in these necroses in the liver.

ACUTE YELLOW ATROPHY OF THE LIVER (ACUTE NECROSIS)

Acute yellow atrophy is an acute and widespread autolytic necrosis of the liver cells, characterized clinically by jaundice, reduction in the size of the liver, and toxic disturbances of cerebration, proceeding to a fatal issue. The disease is comparatively rare. The earliest record of a case is by Ballonius (died in 1616). The best recent study is by Miller and Rutherford.[4]

Etiology.—Acute yellow atrophy is especially frequent between the twentieth and the thirtieth year (50 per cent. of the cases), and in women (two-thirds of the cases); both are explainable largely by the frequent occurrence of the disease during pregnancy. Hunter's studies show that more than 80 per cent. of the cases occur between the tenth and the fortieth year; Rolleston collected 42 cases occurring within the first ten years of life. Almost one-half of the cases in women, that is about 30 per cent. of all cases, occur about the middle or during the latter half of pregnancy; the disease is scarcely if ever seen during the first three months of pregnancy, but sometimes it occurs during the puerperium. The onset in pregnant women has been preceded by shock, fright, mental disturb-

[1] Consult McCrae: *Jour. Path. and Bacteriol.*, Cambridge, 1908, **12**, 279.
[2] *Jour. Med. Research*, 1904, **12**, 75; *Jour. Exper. Med.*, 1906, **8**, 103.
[3] *Jour. Exper. Med.*, 1907, **9**, 64.
[4] *Quart. Jour. Med.*, 1923–1924, **17**, 81 (literature and illustration).

ances, and anxiety (related or not to the pregnancy and expected parturition), all of which are believed to exert some influence; but it is extremely unlikely that these do more than depress the general resistance. The causative influence of pregnancy is much more likely akin to that exerted by the toxemias of pregnancy, in which the liver frequently shows degenerative changes, and in the production of which it plays an important, according to some observers the important, part. The actual etiological factor, however, is not known, since the disorder does not occur more commonly than once in 28,000 pregnancies (Braun). Various known infections exert some influence; thus 10 per cent. of the cases occur during secondary syphilis (in which slight jaundice is not rare). Various pyogenic infections (septicopyemia, osteomyelitis, etc.), typhoid fever, malaria, diphtheria, etc., have antedated the liver disorder. Microörganisms, especially the colon bacillus and pyococci, have been found in some cases, but being absent in most cases it is difficult to believe that they possess etiological significance; they are probably only secondary invaders. Significance is also attributed to certain non-bacterial poisons, such as alcohol, chloroform, phosphorus, etc. More recently, trichlorethane, trinitrotoluene, carbon tetrachloride, arsphenamine, etc., have been found capable of producing acute necrosis of the liver. Chloroform is of undoubted significance, being responsible for the cases of so-called delayed chloroform poisoning.[1] Opie[2] by the administration of chloroform accompanied by intravenous inoculation with *Bacillus coli* produced advanced hepatic cirrhosis accompanied by active new formation of bile ducts. Phosphorus gives rise to a somewhat analogous condition, but the lesions in the liver are not alike in the two disorders. Similar phenomena may develop in the course of other diseases of the liver, such as advanced passive congestion, cirrhosis, cholangitis, etc. All of the foregoing lead to the conclusion that the designation acute yellow atrophy, as well as icterus gravis, comprises a series of diverse disorders that exhibit more or less superficial resemblance. We can separate some of the cases from the main group, such as those due to syphilis, septicopyemia, puerperal eclampsia, phosphorus poisoning, delayed chloroform poisoning, etc., but the definite etiological factor of the major group still eludes us. Miller and Rutherford point out, first, the conspicuous absence of any single constant etiological factor, and second, the frequency with which a number of possibilities is presented.

Pathology.—The liver is much reduced in size and weight, being often one-half or one-third that of the normal (800 to 500 gm. or less). The reduction is usually uniform, although occasionally more marked in the left lobe (possible site of beginning of the process); in other cases there is more or less irregularity, due to varying grades of the destructive process or to attempts at compensatory hyperplasia. The organ is flaccid and has so lost its normal elasticity and resistance that it may be folded or bent upon itself; the capsule is wrinkled and if not thickened shows the liver to be greenish-yellow, sometimes dirty dark grayish in color, with scattered areas more reddish or reddish-brown in color; often

[1] Consult Wells: *Arch. Int. Med.*, 1908, **2**, 589 (literature).
[2] *Jour. Exper. Med.*, 1910, **12**, 367.

small subserous foci of hemorrhage are also visible. On section the liver is dense and resistant; the section surface is mottled—yellowish or yellowish-red areas of varying size and configuration alternating and more or less gradually merging the one into the other. The yellowish coloration is due chiefly, if not entirely, to bilirubin rather than to fatty alterations (the fat content is usually not increased, and may be diminished); the reddish areas seem to be an advanced stage of the yellow, and to be more numerous or larger the longer the patient lives.

Histologically the appearances vary with the stage of the disease. There is intense and widespread (not focal) destruction of the liver cells, which usually begins at the periphery and spreads to the centre of the lobules; early the cells are somewhat swollen and roundish in outline, but they soon become pale and granular, lose their outline, shrink, and stain poorly and diffusely, and the nuclei become obscured or dissolved. Usually they exhibit a yellowish color (staining with bilirubin). Ultimately the cells disappear, apparently in consequence of autolysis, and leave behind the supporting framework of the liver, granular debris, and endothelium of the capillaries (the reddish areas on macroscopic inspection). So extreme may be the destruction of the liver cells that the microscopic section can scarcely be recognized as liver tissue. Should the disorder be more or less protracted, a variable amount of new connective tissue is formed. In some specially protracted cases there are conspicuous evidences of attempts at regeneration (compensatory hyperplasia) of the liver cells,[1] with proliferation of the bile ducts and lengthening of these channels in an attempt to seek out the new liver tissue.

All the organs are more or less bile-stained. The spleen is soft, and is slightly or moderately, but not extremely, enlarged in about two-thirds of the cases. The kidneys are enlarged, softened, pale, opaque, and often reveal small foci of hemorrhage, cloudy swelling, and fatty changes. The heart also is swollen, softened, pale, and opaque (parenchymatous and fatty degeneration). The gastro-intestinal tract shows the lesions of catarrhal inflammation. Small hemorrhages are found beneath the skin and the various serous and mucous membranes, and are doubtless attributable to toxic changes in the blood and bloodvessels. Hemorrhages may occur also in the brain, and degenerative changes may be seen in the spinal cord. The blood itself is more fluid than normally, coagulates with difficulty, and readily stains the endothelium and adjacent tissues.

Miller and Rutherford indicate that there are three types which present distinctive features and represent different stages. They suggest the terms: (1) Acute atrophy; (2) subacute atrophy; and (3) multiple nodular hyperplasia of the liver. They fully describe the differences in pathological features. Etiologically they incline to an enterogenic poison of high toxicity, although the actual cause is undetermined. They find jaundice is always present in the acute and subacute cases, but may be either present or absent in the multiple nodular hyperplasia ones. Epplen[2]

[1] Consult MacCallum: *Johns Hopkins Hosp. Rep.*, 1903, **10**, 375 (literature).
[2] *Arch. Int. Med.*, 1922, **29**, 482.

believes that some of the findings in Laennec's cirrhosis of the liver indicate that they may represent the regenerative or reparative effects of the milder forms of acute yellow atrophy which have not resulted in immediate death.

Studies of the chemistry of the liver by A. E. Taylor,[1] Wells,[2] and others show that not only is the fat content not increased, but that it may be actually diminished; this specially serves to distinguish the disorder from phosphorus poisoning, of which fatty changes constitute a conspicuous feature—30 per cent. as contrasted with 5 per cent. in acute yellow atrophy. In phosphorus poisoning the liver is enlarged, as a rule, whereas in acute yellow atrophy it is usually lessened in size.

Pathogenesis.—There are several conspicuous features of acute yellow atrophy that endow it with special characteristics: the rapid and marked reduction in size of a large solid organ, the speedy absorption of much of the necrotic cellular debris (in contrast with other forms of necrosis), and the appearance in the urine of leucin, tyrosin, and other amino-acids, products of destructive protein metabolism that do not occur in health. These seem unquestionably to point to the activity of some poison, virulent in nature and possessing a special affinity for the liver, upon which it acts widely and intensely. The source, nature, and exact mode of action of this poison are not definitely known. F. W. White[3] supports the view, originally advanced by Flexner,[4] that the process is autolytic in nature, and that it is brought about by some poison having a specific action on the liver cells whose life it destroys without injuring the proteolytic ferments they contain, whence autodigestion ensues. The leucin and tyrosin result partly from autolysis of the liver, and partly from non-conversion into urea of leucin and tyrosin formed elsewhere. Other evidence of this autolysis is found in the albuminose and purin bodies (destruction of nuclein) sometimes encountered in the urine.

The jaundice is due to obstruction of the small biliary ducts by swollen and desquamated epithelial cells and by pressure from without exerted by swollen and necrotic liver cells; it is contributed to by destruction of erythrocytes and the formation of bile thrombi. The presence of bilirubin in the blood and the urine suggests that there may be some alteration in the bile pigment-forming function of the liver.

Symptoms.—The initial symptoms are those of gastro-intestinal catarrh, soon (one to four days) followed by jaundice; these may last a variable period, usually five to seven days, but sometimes several weeks. During this period the disorder is usually looked upon as ordinary catarrhal jaundice (cholangitis), and as a matter of fact there is little if anything to suggest the more serious disorder. The patient complains of malaise, perhaps fugitive neuromuscular pains, poor appetite, coated tongue, occasional vomiting, constipation, etc.; there is usually moderate jaundice and bile-pigment in the urine. Soon, however, the graver symptoms supervene. The jaundice deepens, becoming dark yellowish

[1] *Jour. Med. Research*, 1902, **3**, 424.
[2] *Jour. Exper. Med.*, 1907, **9**, 627.
[3] *Boston Med. and Surg. Jour.*, 1908, **158**, 729 (literature).
[4] *Am. Jour. Med. Sci.*, 1903, **126**, 202.

or bronze-like, slightly greenish (in rare, extremely rapid cases jaundice may be absent); severe nausea and vomiting set in and are often associated with hematemesis; diarrhœa may supervene; and grave nervous symptoms ensue—headache, photophobia, mental confusion, hebetude, and restlessness, soon followed by a noisy delirium, and later coma and perhaps convulsions. Hemorrhages (disordered nutrition of the vessel walls and hemolytic action of bile salts on the erythrocytes) occur beneath the skin and into and from divers mucous membranes (intestines, urinary tract, respiratory tract, genital tract, retina, and most commonly the stomach); absorption usually occurs in pregnant women. Soon the patient passes into a profound typhoid state. There may be slight fever (pyogenic infection?), but usually the temperature is below normal (until shortly before death, when there may be an agonal rise); the pulse becomes rapid, feeble, and of low tension; the respirations become accelerated and irregular; the pupils dilate (said to be important diagnostically); the tongue becomes dry, furred, and tremulous; sordes collect on the teeth and gums; and there are fibrillary twitchings.

The *liver* in some cases is found slightly or moderately enlarged in the early stages; this may be due to preëxisting disease (as cirrhosis), but rarely it seems to be a part of the acute yellow atrophy itself. Soon, however, the liver dulness diminishes rapidly in extent, until it may be entirely absent or constitute a small area in the axillary region; this is due to reduction in the size of the liver and to the fact that the small flabby liver falls away from the anterior abdominal wall and is replaced by the intestine. Death may occur before the liver lessens in size. The region of the liver may be tender on pressure. Slight or moderate enlargement of the *spleen* may be made out in about two-thirds of the cases; in the event of unusual hemorrhage or diarrhœa the spleen usually remains small.

The *urine*, as a rule, is lessened in amount, of increased specific gravity, of increased acidity, and highly colored (bile pigment and excess of urobilin); it usually contains a small amount of albumin, and hyaline, granular, fatty, and epithelial tube casts. The highly significant changes consist in the presence of leucin, tyrosin, and the other amino-acids (largely the result of autodigestion of the liver); sarcolactic, diacetic, and other fatty acids (lactic, acetic, butyric, and succinic); marked reduction in the amount of urea with an associated increase in the amount of ammonia and other nitrogenous substances. Sugar is rarely found. The amount of leucin and tyrosin is no index of the amount formed in the body (in the liver and elsewhere), since both substances are comparatively insoluble, and despite elimination, considerable of both substances may be found in the liver after death.

Examination of the blood often reveals a normal or an increased number of erythrocytes (usually attributed to concentration of the blood); leukocytosis (up to 16,000) and a moderate reduction of the hemoglobin (60 to 80 per cent.). Bile pigments also may be found.

Diagnosis.—In the early stages there is scarcely anything to distinguish the cases from catarrhal jaundice, although jaundice and an enlarged and tender liver in a pregnant woman are of portentous significance.

Careful studies of the urine, especially in pregnant women, and in cases of mild jaundice, and the detection of significant urinary changes, especially the evidences of an acid intoxication, should enable us to recognize the antecedent conditions and perhaps ward off the more serious later stages. The development of nervous symptoms in any case of jaundice should always awaken suspicion. When fully developed, jaundice, vomiting, delirium (and other cerebral symptoms), lessening in the size of the liver, and the presence of leucin and tyrosin in the urine are unmistakable. The presence of leucin and tyrosin is not unequivocal, since both substances may be found in small amounts in the urine in other diseases, such as afebrile jaundice with slight enlargement of the liver, leukemia, erysipelas, typhoid fever, etc., and lessening in the size of the liver may be missed in those cases with cirrhosis (with a small liver), or when the liver is bound to the abdominal wall by adhesions.

Phosphorus poisoning may be excluded by the absence of a history of the ingestion of phosphorus (not always trustworthy), the later development of jaundice (in phosphorus poisoning usually after a day or two of symptoms referable to disordered stomach), decrease in the size of the liver (which usually remains enlarged in phosphorus poisoning), the more severe nervous symptoms, and the occurrence and larger amounts of leucin and tyrosin. *Biliary cirrhosis* may be excluded by the presence of an enlarged liver with jaundice and fever, the absence of leucin and tyrosin from the urine, and the longer course.

Prognosis.—The disease runs a somewhat variable course. In a majority of the cases death ensues before the fourteenth day; almost half of the cases terminate fatally in from the fifth to the tenth day; a few cases become chronic and may last upward of four or six to eight weeks; rarely, but apparently undoubtedly, recovery may ensue, in which event the disorder is of much protracted course. Death before the fifth day is uncommon, except in pregnant women. The prognosis is extremely unfavorable, virtually fatal, the rare recovery serving rather to accentuate the ordinary course of the disease than to hold out hope of recovery in any particular case. The prognosis is especially bad in pregnant women, also in all cases, the more violent in nature and the earlier the onset of the nervous symptoms, in the event of serious renal complications, such as oliguria, albuminuria, casts, decrease in nitrogen excretion (evidences of toxic retention or acid intoxication), and in cases with severe hemorrhages. Virtually the prognosis depends upon the severity and length of the second stage of the disease; rarely this lasts more than two or at the most three days; should the symptoms be mild or abate, hope of ultimate recovery may be entertained, but usually the disorder becomes chronic and the patient eventually dies. The possibility of recovery, however, cannot be denied.

Treatment.—The extraordinary mortality shows the futility of therapeutic endeavors, nor can we hope for improvement until time and research have disclosed the cause. Perhaps it is too much to expect that we should view every case of jaundice as likely to eventuate in acute atrophy; but jaundice in a pregnant woman is assuredly serious, and should be looked upon as a possible forerunner of acute yellow

atrophy. It is wise in all cases of jaundice in pregnant women (as well as in all cases of so-called catarrhal jaundice) to study the urine for evidences of acid intoxication and destructive protein metabolism, and, should this be found, to institute appropriate treatment. Chloroform and chloral should be used cautiously in pregnant women, especially in treating convulsions.

In the early stages the patient should be confined to bed. Milk is the best food, and should be diluted with some alkaline mineral water; cereals and other carbohydrates may be given in considerable amounts, since they are likely to prevent or limit the acid intoxication. The bowels should be opened freely; calomel and the saline cathartics seem the best. Insistence should be laid upon the drinking of large amounts of water; any good water will suffice, but an alkaline mineral water is probably preferable. Alkaline diuretics may be added to the water or given otherwise. If hypoglycemia is found, 200 to 500 cc. of 5 per cent., 10 per cent. or even 25 per cent. solutions of glucose should be given intravenously and repeated every four to eight hours if the blood sugar again falls. A solution of 2 per cent. sodium bicarbonate and 5 per cent. glucose should be given by proctoclysis, 500 to 1000 cc. every four, six or eight hours. In an early stage, duodeno-biliary drainage might be tried in the hope of removing part of the toxic factors in the bile.

The principles in the second stage are similar to those of the first—to prevent or limit the formation and to promote the elimination of toxins. The measures mentioned should be continued, and free catharsis and diuresis maintained; otherwise the treatment is symptomatic.

CONGESTION OF THE LIVER

The liver is responsive to variations in the inflow of portal blood on the one hand, and the outflow of the general systemic venous blood on the other hand; to these must also be added its responsiveness to the supply of arterial blood. The amount of blood within the liver, therefore, is subject to wide variations in health, and it varies also in disease with the factors upon which it is dependent. That the liver is capable of accommodating an extraordinary amount of blood is obvious from the great size it often attains when congested, and the very marked reduction in size that may follow relief of the factors provoking the congestion. The increased amount of blood may be due to increased inflow or impeded outflow of the blood—whence we may distinguish an active and a passive congestion, but neither can be looked upon as a disease entity. The one is largely toxic in nature and usually gastro-intestinal in origin; the other is largely mechanical in nature and usually cardiac in origin.

Active Congestion.—Etiology.—This may result from an excess of blood from the portal vein or the hepatic artery; the portal vein is the more important factor. This active congestion develops under a variety of circumstances: (1) It occurs as a physiological process during digestion, when the amount of blood carried to the liver by the portal vein is increased, lessening and finally subsiding as digestion proceeds to its completion. (2) Various poisons, some endogenous, some exogenous,

may be carried to the liver by the portal vein and provoke acute congestion. (3) Active congestion may also result from the action of the toxins of certain infections that may reach the liver by way of the general circulation, such as pyococcic infections, typhoid fever, yellow fever, etc. In some of these infections the poison may reach the liver by the portal and the general circulation. (4) There is a group of cases presumably of active congestion attributed to the influence of "cold."

It is obvious that many of the aforementioned factors are the causes also of inflammation and of degenerative changes in the liver, and, as a matter of fact, it is difficult in many cases to separate the one condition from the other; indeed, in some cases they are combined. Degenerative changes are very common in all toxemias, and are not uncommonly associated with congestion; and congestion itself is an early stage of inflammatory conditions.

Pathology.—The liver presents the ordinary appearances of active congestion (which, however, after death are ill marked); it is enlarged, swollen, and contains an increased amount of blood, whence it is somewhat dark reddish or reddish brown in color, and it drips blood on section. Microscopically there is dilatation of the capillaries and small vessels of the capsule of Glisson; often there is parenchymatous and sometimes fatty degeneration, occasionally pigmentation of the liver cells. Rarely there is œdema, congestion, and proliferation of the biliary ducts.

Symptoms.—These are rarely unequivocal. Most of the cases follow or are associated with dietetic indiscretions, and the symptoms are largely those of disturbances of digestion, which in general partake of the complex popularly designated "biliousness." In consequence of an excess of food or too much alcohol, excessive demands are made upon the liver. The appetite is poor, temporarily lost, the sight or thought of food often exciting disgust; there is a bad taste in the mouth and the tongue is furred; there is epigastric distress, which sometimes amounts to pain and is usually aggravated by taking food; nausea is common and vomiting may supervene; there is often discomfort and sometimes pain in the region of the liver, which rarely is referred to the right shoulder and scapula, increased by deep breathing, sudden movement, and lying on the side; usually there is constipation and the stools may be light colored, but there may be transitory diarrhœa. There are general malaise, headache, sometimes vertigo, a feeling of nervousness with unrefreshing sleep, irritability, depression, etc. Occasionally there is slight jaundice, more often a peculiar sallowness of the face and skin. The liver is enlarged and tender, but the enlargement is not marked. The urine is commonly concentrated, of increased specific gravity, and deposits an abundant sediment of urates; occasionally there is a transitory (toxic) albuminuria. Bile pigments are present in the event of jaundice. The disorder is usually afebrile, although there may be a rise in temperature to 100° F. or thereabouts (in which event the disorder should be viewed as having progressed to acute parenchymatous hepatitis).

In another class of cases, those met with in infections, such as dysentery, etc., the constitutional symptoms are more marked, slight or moderate fever is usually present (progression to acute hepatitis), and

the local gastro-intestinal symptoms are more or less in abeyance, but become aggravated during digestion. The liver is enlarged and tender.

Diagnosis.—This is usually apparent from the etiological factors, the general disturbances of the gastro-intestinal tract, the slight jaundice, and enlargement and tenderness of the liver; by no means of minor diagnostic importance is recurrence of attacks in a person of known ill-chosen habits of eating and drinking. The difficulties consist in determining whether or not to the congestion permanent damage to the liver tissue has been added. With recurrence of attacks, their increasing duration, and lessening intervals, this becomes the more likely; the less the enlargement of the liver and the quicker it subsides (or returns to the normal), the more is permanent damage unlikely. In the more acute cases encountered in infections aggravation of the constitutional symptoms, together with enlargement and tenderness of the liver, usually suffice for diagnosis.

Prognosis.—The disorder rarely lasts more than three or four days; sometimes a week. It is not dangerous in itself, but acquires its importance because of its etiological factors (especially alcohol) and its frequent recurrence in those who persist in the use of alcohol, in whom it is likely to eventuate in cirrhosis, and in those continuously exposed to other etiological factors, such as dysentery, etc., in the tropics.

Treatment.—There is reason to believe that in those who eat and drink too much and lead a sedentary life, in the gouty, those of plethoric habit, and those formerly the subjects of chronic malaria, dysentery, etc., in the tropics, prophylactic measures may serve to ward off attacks, at least recurrences, of acute congestion of the liver; and it is by no means unlikely that appropriate energetic treatment undertaken early in cases of what cannot be called other than acute congestion would often prevent the later development of cirrhosis Obviously the causal factors should be avoided, and one should cultivate abstemious habits. The food should be moderate in amount and easily digested; highly seasoned articles should be avoided; alcohol should be omitted altogether or taken only occasionally, as whisky in small amounts, well diluted, and with the meals. The body, especially the abdomen and back of the neck, should be protected from "cold" by day as well as by night. Constipation should be overcome, preferably by laxative foods, an occasional mercurial purge, and the saline cathartics. A sedentary life should be at least partially replaced by activity. Golf or horseback riding are usually good choices.

When the attack has developed the patient should go to bed and be kept there until convalescence is complete. The guiding principle should be to reduce the functional demands upon the liver, to eliminate all factors that might provoke or add to its congestion, and to reduce any existing intestinal catarrh. These objects are best achieved by dietary regulations. The diet should be minimal in amount and absolutely unirritating; in general it should consist exclusively of milk, which should be given at stated (rather long) intervals, and well diluted with lime-water or other alkaline water. Whey, junket, albumin water, strained broths (without seasoning), barley water, calf's-foot jelly,

etc., may be given later, and, indeed, early to those who seriously object to or are inconvenienced by milk. Gradually the diet may be augmented, at first by the addition of cereals, and then meat, etc. Alcohol must be absolutely interdicted. Plain or alkaline water should be given in large amounts throughout. The congestion of the liver and the intestinal catarrh are influenced by free saline purgation.

Ammonium chloride (20 gr.–1.3 gm.—thrice daily) has long enjoyed a reputation in disorders of the liver. It may be given in the early stages, with the alkalis (alkaline waters, sodium bicarbonate, etc.), or later with nitrohydrochloric acid, nux vomica, or strychnine, and a bitter tonic. The distressing gastric irritability may be controlled by sodium bicarbonate, bismuth subnitrate, and carbolic acid. Local measures, such as cold compresses, etc., sometimes relieve the local discomfort.

Those subject to recurrences of congestion of the liver are much benefited by treatment at some of the well-known spas, such as Carlsbad, Marienbad, Vichy, Brides, etc. Many of the waters of our own country, such as Saratoga, etc., are equally efficacious, but there is little if any control of the patient at the resorts, and the accessories are largely wanting.

Passive Congestion.—Etiology.—This is due to factors that impede the efferent circulation; these are largely mechanical in nature and cardiac in origin (whence the name cardiac liver). The disorder occurs: (1) In failure of the heart, whether acute or chronic. (2) It occurs also in the advanced stages of such diseases of the lungs as cause increased work of the right side of the heart and ultimately lead to its failure, such as emphysema, chronic bronchitis, asthma, chronic adhesive pleuritis, and compression of the lungs (by pleural exudates, mediastinal tumors, aneurisms, etc.). (3) It may result also from local factors that obstruct the circulation about the junction of the hepatic veins and the inferior vena cava, of which the most important are kyphosis and scoliosis, tumors, gummas, etc., of the liver, inflammatory bands and adhesions, and kinking of the hepatic veins or the inferior vena cava by a displaced heart or a large pleural or peritoneal effusion.

Pathology.—Passively congested livers may be divided into three classes, more or less distinct, but representing different stages of the same process: (1) The merely congested or engorged liver, found in cases of acute or recent heart failure (common in the infections, such as pneumonia, typhoid fever, etc.), and in chronic valvular disease with well-maintained compensation in which death has occurred suddenly or after a few days' illness only; (2) the congested nutmeg liver, found in cases of long-standing heart disease with dilatation of the right heart and tricuspid insufficiency, in which compensation, although precariously maintained, has been on the whole fairly satisfactory, and in which no serious or prolonged failure has occurred until that which leads to death; and (3) the fibrotic nutmeg liver, found also in cases of long-standing heart disease with dilatation of the right heart and tricuspid insufficiency, in which one or more severe and prolonged attacks of failure of compensation have occurred, during which the auricle has suffered especially and, being perhaps totally incapacitated, has permitted the full force of

the ventricle to be transmitted to the hepatic lobules with consequent rupture of the venules and capillaries, laceration and destruction of hepatic parenchyma, and its repair by new-grown connective tissue.

The congested liver in the early stages is increased in size, depending upon the amount of contained blood: it is firmer and denser, and dark purplish or bluish in color. On section the liver in the early stages drips blood and presents a more or less uniformly congested dark bluish or purplish color, sometimes slightly mottled with lighter areas; in more advanced stages the excess of blood is less apparent, and the organ presents the characteristics spoken of as the congested nutmeg liver; the intralobular and sublobular venules being distended and overfilled with blood, appear as dark purplish or reddish spots (transverse section) or streaks (longitudinal section), which are in marked contrast to the pale yellowish or whitish circumferential liver cells, the seat of fatty infiltration and biliary pigmentation. When of still longer duration, the liver has decreased in size and may be less than normal; it is firmer and denser, but still presents the nutmeg appearance; about the distended central veins some fine new connective tissue, often pigmented, reddish in color, may be obvious; the hepatic veins are dilated and their walls thickened and opaque; the adjacent hepatic tissue is atrophic and pigmented, and invading it fine fibrous connective-tissue trabeculæ may be detected (fibrotic nutmeg liver; red atrophy of the liver). The capsule is sometimes thickened and opaque, especially in the event of ascites, and through it the distended subcapsular veins may be apparent. In some cases there may be a more or less universal perihepatitis, commonly associated with pericarditis and pleuritis (so-called multiple serositis). More or less extensive hemorrhage into the centre of the lobules and consequent destruction of the hepatic parenchyma are not uncommon. The hepatic cells about the central veins show a variable degree of atrophy—partly a pressure atrophy and partly doubtless nutritional, the result of insufficient oxidation or due to toxins or cytolytic ferments. In most cases there is a considerable accumulation of fat in the liver cells; usually, also, the cells about the central venules contain more or less pigment derived from the hemoglobin, usually hematoidin, but also hemosiderin. In consequence of atrophy of the liver cells the supporting reticulum becomes relatively increased, and it becomes absolutely increased in consequence of new growth (replacement fibrosis). This fibrosis is usually most marked about the central vein, and it gradually radiates therefrom, following the capillaries throughout more or less of the lobule. There is always more or less fibrosis about the hepatic veins and about the portal veins also some fibrosis may be observed, but this is always minor in grade and disproportionate to the fibrosis elsewhere. The capsule is usually thickened, and from this new connective-tissue trabeculæ usually invade the liver to join the new perilobular connective tissue.

The new-growth of fibrous tissue has led to its comparison with cirrhosis, and the term *cardiac cirrhosis* has been employed. But the lesions are in no way comparable to those of ordinary cirrhosis. The slight fibrosis common in the congested nutmeg liver is intimately related

to the central and sublobular and hepatic veins; it results no doubt from the chronic distention of the veins; but the more marked fibrosis in the fibrotic nutmeg liver is doubtless in large part a replacement or scarring process, to repair destroyed liver parenchyma. Such periportal fibrosis as occasionally occurs is purely subsidiary, and may readily be accounted for by the fact that hepatic vein obstruction may lead to portal congestion, which in turn sets up chronic intestinal catarrh; the poisons thus induced may be transported by the portal vein to the liver and induce a mild grade of portal cirrhosis; in many cases of chronic heart disease, alcoholism is quite common, and may set up an ordinary cirrhosis; and finally, many cases of ordinary portal cirrhosis have added passive congestion. The phenomena should be correctly interpreted; the liver in passive congestion rarely presents the lesions of true cirrhosis.

Symptoms.—These consist of (1) those due to the primary cardiac or pulmonary disease; and (2) those due more directly to the disorder of the liver itself, which consist of local distress and gastro-intestinal phenomena. The severity of the local subjective symptoms often depends more upon the rapidity of the development of the congestion than upon its grade; that is, subjective symptoms may be for some time in abeyance if the congestion develops slowly, although it may reach a high grade; whereas a less grade of congestion, developing rapidly, may occasion considerable distress. In one class the manifestations of cardiac failure predominate; in another class, phenomena referable to the liver predominate.

Chief among the local symptoms are pain, superficial and deep tenderness, and distress or a sense of weight and heaviness in the right hypochondrium, aggravated by pressure, motion, deep inspiration, and the lateral posture. The congestion in the hepatic veins leads to congestion also in the portal tributaries, with consequent disturbances in digestion, poor appetite, epigastric distress, especially after eating, flatulence, nausea, constipation, etc. *Jaundice* is a common phenomenon; usually it is slight or moderate in grade, in which even the admixture of cyanosis and jaundice lends a very characteristic bluish-green or greenish-blue discoloration. The jaundice may be due to compression of the biliary capillaries and consequent interference with the flow of bile; perhaps more commonly to radicular cholangitis; or to the extension of the intestinal catarrh to the diverticulum of Vater and the common bile duct, in which event the obstruction is rarely complete. In rare instances a terminal infection leads to marked increase of the jaundice (sometimes associated with mental symptoms, icterus gravis), doubtless due to toxic destruction of the hepatic cells. Helpful differentiation as to the type of jaundice and its cause, may be made by the van den Bergh test for bilirubin in the blood serum. Œdema and ascites are common. The œdema is usually preceded for some time by enlargement of the liver, except in cases in which there is a sudden and severe cardiac collapse. Œdema does not supervene until the liver has exerted to the utmost its safety-valve action, and the readiness with which œdema appears and disappears is a tolerably accurate indication of the functional activity of the liver in this respect. The ascites may be part of a general dropsy and due solely to the factors provoking the anasarca, in which event it

is likely to be small in amount, proportionate to the œdema; or it may be disproportionate, large in amount, and require frequent tappings; in this event it is associated with the fibrotic congested liver, or with chronic adhesive peritonitis (perihepatitis) or a more generalized peritonitis. An acute peritonitis may supervene, with audible and palpable friction.

Examination of the liver reveals it to be enlarged; the size varies from time to time, depending upon the condition of the heart. The organ may be palpable a full handbreadth below the costal margin; it is uniformly smooth, has a sharp or slightly rounded edge, and is usually more or less tender. In advanced stages the liver becomes reduced in size (reduction in the amount of blood, cicatrization of connective tissue, atrophy of parenchyma), and may no longer be palpable. The enlarged liver not infrequently pulsates. The pulsation is more likely to be found in early stages, before new-grown fibrous tissue interferes with expansion of the organ. The enlarged liver causes displacement and compression of adjacent organs; it may cause collapse of the base of the right lung, with dulness on percussion and feeble or absent breath sounds (which should not be mistaken for pleural effusion).

The urine is concentrated, of high specific gravity and high color; it contains an excess of urobilin, and usually a small amount of albumin. The albuminuria is proportionate to the cardiac debility, and disappears with improvement in the cardiovascular condition.

Examination of the bile recovered by duodenal aspiration will usually show definite evidence of the associated biliary-tract catarrh and stasis.

Diagnosis.—This is usually evident from a knowledge of the primary disorder, an enlarged and tender liver, and other evidences of failing cardiac compensation. The enlarged and congested liver may usually be readily distinguished by the fact that its volume changes considerably from time to time, which does not obtain in the case of other enlarged livers, and that lessening in the size of the liver is commonly associated with other evidences of improved cardiac tone and an increase in the amount of urine. Congestion may be distinguished from *cirrhosis* of the liver by evidence of the primary cardiac or pulmonary disorder, other evidences of failing heart, a smooth liver, the absence of dilated abdominal veins, and by the response to medication directed to the condition of the heart; but one must remember that congestion is not uncommon in cirrhosis of the liver, and that the marked reduction in the size of cirrhotic livers is often due to lessening of congestion rather than to atrophy of hepatic parenchyma. The smooth surface and varying size of the liver, responding to treatment directed to the heart, and the absence of cachexia will usually serve to exclude malignant disease; absence of the etiological factors will usually exclude amyloid disease; and an examination of the blood will exclude leukemia.

Prognosis.—This depends altogether upon the primary disease and the response to treatment of the provoking cardiac disorder.

Treatment.—The treatment is that of the primary cardiac or pulmonary disorder causative of the hepatic congestion; virtually, whatever the primary disease, the treatment is that of failing cardiac compensation. The patient must be absolutely at rest so as to reduce the work of the

heart. The diet should be light and nutritious; fluids should be small in amount. Digitalis is the sovereign remedy. The Addison, or Guy's pill, consisting of digitalis, squill, and mercury (calomel or blue mass), is valuable in many cases. Diuretics, such as theocin, the potassium salts, etc., may be given with hope of benefit. Bleeding is often efficacious.

The hepatic congestion is also favorably influenced by cathartics, especially the salines, which should be given in quantity sufficient to caiuse free watery movements. The vegetable cathartics also are useful, especially in connection with a relatively dry diet, for several days, from time to time. Pain in the region of the liver may be relieved by hot compresses, an ice-bag, etc. General nervousness and insomnia are often markedly benefited by morphine hypodermically: $\frac{1}{32}$ to $\frac{1}{16}$ gr. (0.002 to 0.004 gm.), usually suffices and is quite as efficacious as larger doses. Œdema may require punctures and ascites may require repeated tappings. The tapping should not be too long delayed if the patient suffers much distress; on the other hand, it should not be performed too rapidly, not too much fluid withdrawn, since the removal of the pressure sometimes permits the rapid absorption of toxic substances and leads to the development of uremic manifestations. *Novasurol*[1] has been found of value because of its pronounced diuretic action, especially when combined with ammonium chloride and a low fluid, low salt diet. Ammonium chloride is given by mouth in divided doses up to 10 gm. daily, best in the crystalline form in capsules of 0.75 gm. or 1.50 gm. The use of these measures may relieve the ascites without tapping.

Duodenal drainage of the biliary tract, (especially in regard to "C" or liver bile) is a most useful procedure in recurrent congestion of the liver, both in the acute and chronic forms. In the latter, due regard must be given in the selection of the individual patient as to the balance of reserve of cardiac muscle. If not too greatly disturbed such drainage can be carried out with safety and will be followed by improvement.

PERIHEPATITIS

Acute Perihepatitis.—Etiology.—This is almost, if not quite, without exception a secondary disorder. Rarely it follows trauma of the right side (contusions, fractures of the ribs, etc., with or without contusion or laceration of the liver and its capsule); in the great majority of cases the perihepatitis is secondary to disease of the liver or adjacent viscera. It occurs in association with acute congestion and inflammation of the liver (especially in the tropics); it is not uncommon in long-standing passive congestion; it occurs in various forms of suppuration within the liver; it is associated with tubercles, gummas, and rapidly growing new growths of the liver that reach to or project beyond the surface; it follows inflammatory and ulcerative processes in adjacent organs, such as ulcers of the stomach, duodenum, and other parts of the intestine, cholecystitis, pancreatitis, appendicitis, etc., in which circumstance the lesions ultimately often are those of one form of subphrenic abscess; it may

[1] Rowntree, Keith and Barrier: *Jour. Am. Med. Assn.*, 1925, **85**, 1187.

be part of a general peritonitis; and it may follow disease of the thoracic viscera (pleuritis, pericarditis, etc.) through extension through the diaphragm. Acute perihepatitis is obviously always the result of infection; the common infecting agents are the pyogenic cocci (staphylococci and streptococci), the pneumococcus, the colon bacillus, etc.

Pathology.—The lesions may be localized or diffuse, and fibrinous, serofibrinous, or purulent in character. Early the peritoneum loses its lustre and becomes dull and opaque, the vessels become injected, and a small amount of serum or serofibrin is thrown out. The lesions may not extend beyond this: the serum becomes absorbed and the fibrinous exudation undergoes organization, with the ultimate formation of filamentous or dense adhesions. The lesions vary in situation with that of the primary cause: in traumatic cases, and those associated with various diseases of the liver itself (abscess, gummas, new growths, etc.), and of the thoracic organs, the lesions are most likely to be on the antero-superior surface of the liver, and the ultimate adhesions bind the liver to the diaphragm and the anterior abdominal wall; in the cases that follow disease of the adjacent abdominal organs the lesions are most likely to be at the contiguous, usually inferior, surface of the liver; in cases due to transport of infection from a distance (appendicitis for instance) the lesions are most common on the superior aspect of the organ; but most unlooked-for lesions sometimes occur. In other cases the lesions progress to suppuration.

Symptoms.—The important clinical phenomena consist of local pain and audible and palpable friction, which are quite similar to the analogous pleuritis. The pain is often acute and lancinating; it may be located anywhere in the region of the liver, but it is not infrequently referred to the margin of the ribs and the epigastrium (fairly widespread perihepatitis), or rather high up in the axilla (more localized peritonitis), and it frequently radiates to the supraclavicular fossa (said by Cantlie to be diagnostic); it is made worse by motion, such as deep inspiration, or the lateral posture, or by passive motion made by the physician. The movements of the right lower chest are restricted or abolished. Palpation reveals local tenderness and not infrequently rigidity of the upper abdominal muscles on the right side. Auscultation may reveal friction which, however, is often quite localized and very fleeting; rarely it may be palpated. Sometimes there is slight or moderate fever; there may be a short, hacking, dry cough sometimes set up by manipulations of the liver. Hiccough (suggesting involvement of the diaphragm) is not uncommon and may be severe. Nausea and vomiting may occur in case the stomach, duodenum, or gall-bladder are implicated in the inflammation. Occasionally slight ascites develops—due to interference with drainage of the peritoneum through the diaphragm; this is quite independent of the marked ascites due to general peritonitis, etc.

Diagnosis.—This is not infrequently obscured by the predominance of symptoms of the primary disorder; sometimes the lesions are found after death in cases in which no noteworthy symptoms were present during life. However, the diagnosis can usually be made by noting the symptoms of the primary disorder, and in addition local pain and tender-

ness, audible and sometimes palpable friction, and perhaps rigidity of the abdominal muscles of the right upper quadrant. The condition is probably most commonly mistaken for right-sided pleurisy—which may coexist; the acute perihepatitis, however, can usually be distinguished by a knowledge of the primary (usually abdominal) disorder, the lower situation of the local signs, and the onset of severe pain upon passively moving the liver forward and backward (Cantlie).

Prognosis.—This depends upon the primary or underlying condition; the acute perihepatitis (unless it progresses to suppuration), although distressing, is not in itself dangerous to life.

Treatment.—The treatment is that of the primary disease; but in some cases the phenomena of the acute perihepatitis so overshadow those of the primary disease as to furnish the indications for treatment. Pain often demands immediate attention and may be relieved by strapping the side; this may obviate the necessity of giving opium, which should not be withheld should the pain continue. In some cases more or less relief attends the use of poultices, an ice-bag, dry cupping, leeches, and other forms of counterirritation, etc. The patient should be kept at rest and on a light diet until the acute manifestations have subsided.

Local Chronic Perihepatitis.—Etiology.—This not infrequently follows acute perihepatitis, particularly repeated attacks, and it is due, therefore, to the same causes. It is perhaps most commonly found in association with chronic passive congestion of the liver (long-continued expansion and contraction of the liver with consequent peripheral friction), pressure atrophy (corset liver, etc.), gummatous and tuberculous new formations, tumors and hydatid cysts reaching the surface of the liver, chronic cholecystitis, gastric and duodenal ulcers, etc.

Pathology.—In many cases local chronic perihepatitis represents the process of healing of acute perihepatitis by the formation of adhesions, in which event the process is obsolete, non-progressive; the adhesions are firm, fibrous, and non-vascular; they are attached to, and virtually form a part of, the capsule of the liver; and they serve to bind the liver to adjacent structures and tissues—the diaphragm, the gall-bladder, the anterior abdominal wall, the stomach, duodenum, pancreas, intestine, omentum, etc. In some cases adhesions have not formed, the capsule of the liver revealing here and there more or less localized thickenings, much resembling the so-called milk spots of the pericardium. Rarely there appears to be some progression from the local to the general form of perihepatitis, but, as a rule, the two are quite distinct.

Symptoms.—These are scarcely, if ever, definite; but local pain, tenderness, and rigidity, particularly if recurrent, may suggest the disorder; confirmation may rarely be obtained by eliciting audible or palpable friction. In some cases the diagnosis may become apparent by the onset of an acute exacerbation. In the majority of cases the diagnosis is not likely to be made—which is a matter of little or no moment, since the disorder is of comparatively little clinical importance.

Treatment.—This is altogether that of the primary disorder. In rare instances in which the chronic perihepatitis can be diagnosed, and the still rarer instances in which special treatment seems indicated, the measures mentioned in acute perihepatitis are appropriate.

General Chronic Perihepatitis; Chronic Hyperplastic, Hyaline, or Deforming Perihepatitis; Sugar-iced Liver (Zuckergussleber); Multiple Serositis; Polyorrhymenitis; Pericarditic Pseudocirrhosis of the Liver (Pick).—This is a disorder first described by Van Deen, later studied by Curschmann, who gave to it the name of Zuckergussleber (sugar-iced liver), and Hale White, Nichols, Rolleston, etc.[1]

Etiology.—General chronic perihepatitis is about equally common in the two sexes; it occurs at all ages, but is most common in the second and the fifth decades. The exciting causes are ill understood; most likely they are toxic in nature, but the nature and source of the toxin are not known. The rather common association of the condition with arteriosclerosis and chronic interstitial nephritis (19 of Hale White's 22 cases) suggests that the poison may be allied to that of uremia, but this supposition is somewhat negatived by the rarity of chronic perihepatitis in arteriosclerosis and chronic nephritis. It is not improbable that the arteriosclerosis, nephritis, and perihepatitis may be due to the one cause, unknown as it may be. That the etiological factor is often widespread is shown by the common association of disease of several serous membranes (peritoneum, pericardium, and pleura). The process is best explained upon the assumption of a bacterial toxin that finds in the peritoneum (or other serous membrane), reduced in vitality from any cause (such, for instance, as nephritis), a favorable soil for activity. In some cases this poison may be that of malaria, typhoid fever, or other infections; in other cases it may be syphilitic, although syphilis usually causes only a local perihepatitis; in other cases it is undoubtedly tuberculous, although the lesions are not those ordinarily provoked by the tubercle bacillus; but in many apparently non-tuberculous cases characteristic tuberculous lesions may be detected and the tubercle bacillus may be recovered from the lesions. McWeeney[2] suggests that the bovine tubercle bacillus may be the cause in some cases. In most cases, however, no definite etiological factor can be determined.

Pathology.—At first sight the cases appear to be separable into two classes, those in which the lesions are confined to the peritoneal investment of the liver, and those in which they involve also the serous membranes above the diaphragm (pericardium and pleura); but that this is an artificial division is obvious from the fact that the perihepatitis is often only part of a more generalized chronic peritonitis, and that the ultimate lesions are identical, whether they begin below or above the diaphragm; the condition essentially is a chronic multiple serositis.

The lesions consist of the development of a thick encasement of fibrous connective tissue, whitish, glistening, and much resembling icing, whence the name iced-liver or sugar-iced liver. This may envelop the liver completely, or be limited to, or most marked upon, the upper surface; it may be 5 mm. or more in thickness; it is often of cartilaginous consistency; and it can usually be detached in layers, leaving what appears to be a more or less intact peritoneum (this is quite characteristic, and

[1] A review of the literature with a collection of cases will be found in *Multiple Scrositis*, by A. O. J. Kelly, *Am. Jour. Med. Sci.*, 1903, **125**, 116.

[2] *Trans. Roy. Acad. Med., Ireland*, Dublin, 1906, **24**, 402.

serves to distinguish this from other forms of perihepatitis). This new connective tissue exhibits a marked disposition to cicatricial contraction, so that considerable distortion of the liver ensues, especially the narrower anterior margin. The gall-bladder is commonly embedded in dense adhesions and may be discovered only with great difficulty; usually it is collapsed and contains little or no bile, perhaps a small amount of mucus. The lesions not uncommonly involve the pleura (especially the right), and the pericardium, but also other abdominal viscera; the spleen may be similarly encased in a thick, whitish envelope; the omentum may become thickened, indurated and rolled upon itself, forming a hard, almost unrecognizable mass; the mesentery may become thickened and much shortened, in consequence of which the intestine also becomes shortened and perhaps obstructed. In many cases the most widespread adhesions and distortion of the abdominal organs ensue, giving rise to what has been aptly described as deforming peritonitis. Of 110 cases collected by Picchini (50 observed by himself and 60 from the literature), the peritoneum was involved in all (although this was recognized clinically in only 13), pleuritis was present in 109 cases, in 73 of which it was bilateral; the pericardium was involved in 9 of 50 cases.

In 39 cases collected by Kelly, with special reference to the association of chronic obliterative pericarditis and ascites, the pericardium was obliterated in all (more or less extensively calcified in 10); the right pleura was entirely obliterated in 17, and was partially obliterated or contained fluid in 19 (in 3 the condition of the right pleura was not stated); the left pleura was obliterated in 15, it was partially obliterated or contained fluid in 16, it was normal in 3 (in 5 the condition of the left pleura was not stated); in 28 cases there was chronic perihepatitis, and in 31 cases chronic perihepatitis or chronic peritonitis, or both.

The condition of the *liver* is of much interest. In many cases, aside from distortion and compression, there are no noteworthy lesions—a fact of much importance in determining the pathogenesis of the lesions. In the 39 cases mentioned, the liver was reported as nutmeg in 14, cirrhotic in 8, normal aside from compression in 4, nutmeg and cirrhotic in 4, and in 3 there appeared to be only extension of connective tissue from the thickened capsule into the substance of the organ. In these cases (Pick's pericarditic pseudocirrhosis of the liver) the nutmeg appearance of the liver may well be attributed to a failing heart; these do not include the many in which the pericardium is not involved, and in which congestive changes in the liver are rare, unless there be a failure of the myocardium from other causes. In these cases, although a slight amount of fibrosis may extend from the thickened capsule a short distance into the substance of the liver, cirrhosis in an acceptable sense does not occur; but one must remember that thickening and adhesions of the capsule are not uncommon in advanced cirrhosis. The *spleen* is not infrequently enlarged, especially in the cases associated with chronic pericarditis (23 of the 39 cases). The kidneys usually exhibit the lesions of chronic interstitial nephritis, more so perhaps in the cases in which the lesions are confined to the peritoneum.

Microscopically the encasing is seen to consist of new-grown fibrous

connective tissue, for the most part arranged in lamellæ, and the seat of advanced hyaline degeneration (whence Nichols speaks of the condition as hyaloserositis); there are very few bloodvessels, and a small amount of round-cell infiltration—leukocytes and mast cells. Usually there is a more or less sharp line of demarcation between the new tissue and the underlying capsule of the liver.

The lesions may begin in any one serous membrane, and remain localized there or gradually spread to the others. De Renzi believes that the peritoneum is usually involved first; then the right pleura, and then the pericardium. If, however, the right pleura should be involved first, the disease then extends to the peritoneum, thence to the left pleura and the pericardium. In some cases this mode of progression of the disease is not preserved, as sometimes a pericarditis, usually not diagnosed, develops first. The intensity of the lesions about the liver finds its explanation in the normal circulation in the peritoneal cavity, whereby fluids and foreign particles are carried toward the upper surface of the liver; the lymphatics converge toward the suspensory ligament of the liver and the central tendon of the diaphragm. The attempt on the part of the peritoneum to remove certain noxious agents may result in partial or complete success. In the latter instance the peritoneum may be completely rid of the infective agent, which being carried to the mediastinal lymph vessels and glands, may infect the pericardium or the pleura, giving rise to a primary pleuritis or pericarditis; subsequently the peritoneum, by a descending infection, may become involved. In other cases the attempt on the part of the peritoneum to remove the infective agent being only partially successful, the region about the liver and the under surface of the diaphragm succumbs, and a primary perihepatitis occurs. Subsequently the infective agent may travel through the diaphragm and infect the pericardium or the pleura, or both. The peculiarities of the course and distribution of the lymphatics of this region are also accountable for the much greater involvement of the upper surface of the liver, that is present in most cases. The disease is characterized by the fact that it remains localized to the serous membranes; that it does not implicate the intra-abdominal and intrathoracic organs; that it pursues a remarkably slow and insidious course; that it gives rise to the exudation of large quantities of serofibrinous fluid; and that the fluid portion of the exudate tends to become absorbed, in consequence of which adhesions with obliteration of the serous cavities result.

Symptoms.—The disorder often remains latent for many years, and may be entirely unsuspected during life; in other cases there is often a more or less clear history of the past occurrence of inflammation of one or more serous membranes; and in still other cases it is only examination of the patient that discloses the serous membrane disorder. In the cases with manifest symptoms, the most common are sensations of fulness, oppression, and weight in the upper abdomen; or there may be apparently a sudden onset with acute pain. The abdomen increases in size and may attain very large dimensions—due to ascites. With increase in the amount of ascites, the abdominal wall becomes tense

and the other subjective symptoms aggravated. There may be slight and transitory jaundice. Later, œdema of the legs may develop.

A striking feature is the *ascites*, which is present whether the pericardial and pleural changes are absent, slight, or marked. Aside from ascites, the clinical picture varies somewhat, depending upon the seat of origin of the disease. In some cases the disease is ushered in with acute pericarditis, pleuritis, or perihepatitis, which subsides and leaves the patient apparently well for a number of years. Usually, however the lesions of the pericardium and of the pleura are latent, and the first evidence of the disease is ascites. In some cases of primary pericarditis, slight and transient œdema of the legs may be present early, but this is not observed in many cases, as the pericarditis is usually latent. When œdema is present early it usually soon subsides and does not recur until the ascites has been present for a long time or until shortly before death; except shortly before death it is inconspicuous when contrasted with the excessive ascites. Associated with early œdema, slight swelling of the spleen and disturbances of the gastro-intestinal tract may develop, but these usually subside with the œdema, and the disease, as a rule, is characterized by the entire absence of such symptoms, until failure of the heart supervenes, or until shortly before death. The *ascites* is excessive, necessitates repeated tappings, recurs rapidly after tapping, and may remain stationary (not requiring tapping) for many years. Osler mentions a child in whom tapping was done 121 times, and Rumpf a case in which tapping was done 301 times. The ascitic fluid is amber in color, has a specific gravity above 1.015, as a rule, and contains upward of 3 per cent. of albumin—which suggests its inflammatory nature. After repeated tappings, it may be impossible to draw off much fluid on account of many adhesions. The liver may or may not be palpable (depending upon the presence and the grade of congestion); it is usually not palpable in the late stages. The indurated and rolled up omentum may be palpable as a transverse mass; it should not be mistaken for the lower border of the liver. The general condition remains for a long time but little disturbed. The gastro-intestinal functions, as a rule, are well performed, and emaciation is long postponed. In some patients the urine may reveal the usual changes of chronic interstitial nephritis, or those of passive congestion. In other cases there are the obvious symptoms and signs of arteriosclerosis. Finally, in most cases the heart fails or death may be due to some intercurrent complication, such as pneumonia.

Diagnosis.—Recurrent ascites in a person in otherwise good health, together with the disposition and ability to be up and about between tappings, should suggest the diagnosis. Of special diagnostic significance are a history of a previous attack of pericarditis, pleuritis or perihepatitis; the early occurrence and subsequent disappearance of œdema of the legs; marked ascites with little or no œdema of the legs; an enlarged liver early (this may not occur), and a small and distorted but otherwise smooth liver late in the course of the disease; the absence or very late occurrence of marked enlargement of the spleen; a tendency to the repeated occurrence of attacks of pain, tenderness, rigidity, and possibly palpable and audible friction in the right hypochondriac region—attribu-

table to the attacks of perihepatitis; and the rapid recurrence of ascites after tapping. One should always endeavor to determine whether the lesions are confined to the region about the liver or are more widespread, involving the pericardium and the pleura. In these cases one must endeavor to dissociate the symptoms due to the serositis from those due to failure of the circulation induced by the pericardial part of the serositis and its consequences. In most of these cases prime importance attaches to the recognition of an adherent pericardium.

From *cirrhosis* of the liver the condition may be distinguished by the signs of adherent pericardium; the absence of the etiological factors of cirrhosis of the liver; the slow, insidious, protracted, and intermittent course; the long periods during which the ascites may remain stationary and the patient in good condition; the entire absence or transient presence of slight jaundice; the absence, in most cases, of portal congestion and gastro-intestinal disturbances; in some cases, the association of an enlarged, smooth, and firm liver with marked ascites; and the fact that in many cases the patient survives a large number of tappings. Syphilis may be suggested by the history of past infection and other evidences; but gummas may be present in the liver associated with perihepatitis and ascites without other evidences of the infection. The diagnosis sometimes can only be made by the Wassermann reaction or the therapeutic test. The ordinary *tuberculous peritonitis* is suggested by less exudation, other tuberculous foci in the body, perhaps induration about the umbilicus, and the presence of fever. *Malignant disease* is suggested by irregular, nodular enlargement of the liver, evidence of primary tumor formation elsewhere and a more rapid course.

Prognosis.—This is bad as to eventual recovery, but the patient may live for many years. In more than 70 per cent. of the cases the duration is two years or more; in more than 50 per cent., four years or more; and it may be as long as sixteen years. The general health and strength are maintained for a long time, and the patient may go about his business between tappings. Sooner or later the periods between tappings become less, cardiac failure supervenes, or death results from some infection.

Treatment.—This is almost wholly symptomatic, for little can be done to influence the progress. Diuretics or free catharsis may effect the discharge of the too abundant fluid. Potassium iodide and mercury may be tried when there is evidence or suspicion of syphilis. Tapping must be performed when necessary; usually it has to be done frequently, and although occasionally the fluid remains at a standstill for long periods of time, tapping usually has to be resorted to at gradually decreasing intervals. Permanent drainage subjects the patients to the danger of infection and acute peritonitis. Operative interference, such as the Talma-Morison-Drummond operation, is theoretically contraindicated, and practically has not been attended by any benefit in the few cases in which it has been tried.

ACUTE HEPATITIS

The phenomena to which the term acute hepatitis are applicable may be divided into the suppurative and the non-suppurative forms. The

suppurative form comprises the different forms of abscess, suppurative pylephlebitis, suppurative hepatic phlebitis, suppurative cholangitis, etc. The non-suppurative form comprises a series of most diverse disorders that exhibit all stages of progression, from active congestion to the inflammatory focal necroses of many infections (localized process) and the more widespread process manifested clinically as the different forms of icterus gravis and acute yellow atrophy of the liver.

Acute Non-suppurative Hepatitis.—Etiology.—This may result from the factors that provoke active congestion and parenchymatous degeneration. The most common causes are the toxins of different infectious diseases, exogenous poisons, such as alcohol and phosphorus, and certain endogenous autotoxins possibly of gastro-intestinal origin, etc. The lesions vary with the virulence of the toxic cause, the duration or recurrence of its activity, and the resistance of the liver cells. As a matter of fact, acute hepatitis is uncommon in temperate climates, the different bacterial toxins rarely producing changes surpassing parenchymatous degeneration or cloudy swelling, unless we view as inflammatory the different forms of focal necrosis common in infections that sometimes are surrounded by inflammatory zones. Alcohol, especially if taken in fairly large amounts, undiluted, and at rather frequent intervals, induces, as a rule, only an active congestion, sometimes also more or less parenchymatous degeneration and leads ultimately to cirrhosis.

In the tropics a disorder described as acute parenchymatous hepatitis (tropical liver) is of frequent occurrence; it is most commonly provoked by malaria, but also by dysentery and perhaps other infections. It occurs especially in young adult Europeans, and not uncommonly soon (during the first year) after their arrival in the tropics. Undoubtedly factors other than malaria and dysentery are active, although these may be the exciting causes acting upon a liver reduced in vitality. The influence of immoderate eating (especially of animal food), of alcohol, of exposure to cold and fatigue, may not be overlooked. A potent factor in the production of hepatitis, especially the chronic form, is inflammation and infection of the gall-bladder or appendix, as pointed out particularly by Graham, Heyd, MacCarty and others. Examination of liver sections removed at biopsy in cholecystitis shows the liver definitely diseased (varying grades of hepatitis).

Pathology.—The lesions are most diverse, and no one description could accurately include the manifold variations, combinations of congestion, cloudy swelling, focal necroses, and the vascular and other phenomena of inflammation. The lesions vary from small focal necroses, small opaque areas, scarcely obvious to the unaided eye, to the more complete or universal involvement of the organ. In slight or moderate cases the appearances of the liver are those of active congestion and cloudy swelling; in the more severe cases they vary in grade up to those of acute yellow atrophy. In general one may say that the liver is enlarged, swollen, softened, and rather pale in color; the section surface also is pale and opaque, and not infrequently mottled. Microscopically, in addition to swelling, increased granulation and opacity of the liver cells, and obscuration of their nuclei, dilatation of the capillaries, arterioles,

and venules, one encounters also fatty degeneration and pigmentation of the liver cells, thrombosis of certain capillaries and other small vessels, focal necroses, more or less round-cell infiltration, swelling and desquamation of the endothelium of capillaries, and swelling, œdema, proliferation, and desquamation of the cells of the small biliary ducts. In some (protracted) cases, looked upon by many authors as a subacute form of acute yellow atrophy, there is more or less compensatory hyperplasia of the liver cells. In most cases, other parenchymatous organs, especially the kidneys and the heart, exhibit similar changes.

Symptoms.—The symptoms virtually are those of active congestion, of which acute hepatitis is only an advanced stage. Perhaps, although not necessarily, the symptoms are more aggravated in the inflammatory than in the merely congestive disorder; the liver pain and tenderness are likely to be more marked; nausea and vomiting are more common and usually more severe; the vomited matter partakes of the so-called bilious character (greenish, watery), and not infrequently contains blood—due usually to violent and distressing retching that provokes marked thirst and ultimately may induce marked prostration or collapse; the bowels are likely to be constipated, but the constipation may alternate with a foul, ill-smelling diarrhœa; and the nervous symptoms, such as headache, restless irritability, depression, etc., are usually more marked. Jaundice is scarcely more common or more marked than in active congestion; usually it does not amount to more than a subicteric tint to the conjunctiva or a peculiar sallowness of the general integument. The *liver* is enlarged; sometimes, especially in early cases, notably so, when it may reach as low as the umbilicus; it may also be markedly increased upward, perhaps irregularly so; it is not likely to exhibit much enlargement in advanced cases (due doubtless to the presence of new-grown connective tissue—developing cirrhosis). The spleen is enlarged in the cases due to malaria, but usually of normal size or only slightly enlarged in other cases. The urine, as a rule, is concentrated, high-colored, of increased specific gravity, and deposits an abundant sediment of urates and uric acid; occasionally there is a transitory (toxic) albuminuria. Bile pigment is present in the event of jaundice. That, however, which distinguishes the inflammatory from the congestive disorder is the presence of fever. It is true that slight fever, less than 100°, sometimes attends what is looked upon as congestion merely; but the progression of the one disorder to the other is obvious. A temperature of 100° or more is evidence of the inflammatory nature of the disorder.

In the class of cases difficult to classify, but which exhibit various clinical and pathological relations and graduations to certain types of icterus gravis, the onset of the disorder is sometimes sudden and may be attended by a chill or chilliness and soon followed by fever; vomiting may set in, and may be succeeded by diarrhœa; slight (toxic or hemolytic) jaundice is rather common; the liver becomes enlarged, sometimes irregularly so; and the constitutional symptoms are usually severe.

Diagnosis.—This is usually apparent from the etiological factors and the general symptoms, as narrated. The difficulties are in excluding other disorders, such as the different forms of suppurative hepatitis,

and in the presence of jaundice, the different forms of toxic jaundice and acute yellow atrophy. In the early stages it may and frequently is quite impossible to differentiate between suppurative and non-suppurative hepatitis; in some cases time alone gives the diagnosis. In some cases the one is a later stage of the other, and the suppuration may not be susceptible of recognition until the development of the general phenomena of the condition—irregular chills, fever, sweats, etc. In acute yellow atrophy the constitutional and nervous symptoms are more severe, the liver, at first enlarged, becomes small, the duration is less, and the outcome usually death. Phosphorus poisoning is suggested by the etiology, the enlarged liver, gastro-intestinal hemorrhages, severe constitutional and nervous symptoms, etc.

Prognosis.—The first attack of acute non-suppurative hepatitis, especially as observed in the tropics, usually lasts about a week or ten days, and results in recovery; in some cases, however, suppuration ensues. One attack predisposes to subsequent attacks, and with each recurrence the course and termination are less favorable; the liver may remain more or less enlarged and gradually become cirrhotic, or, as in some primary attacks, the process may go on to suppuration.

Treatment.—The prophylaxis and treatment are as in active congestion of the liver. In addition, in those cases due to malaria, quinine should be administered in good doses; its use is often followed by a notable and rapid diminution in the size of the liver. In the event of recurring attacks the patient should remove from the tropics to a cooler climate. Duodenal drainage of the biliary tract is of value in many cases.

Suppurative Hepatitis.—Suppurative hepatitis, or abscess of the liver, occurs under a variety of circumstances and in several forms. There is some justification for the common division into two classes—the large, single, so-called tropical abscess, and the small, multiple, non-tropical abscesses; but the processes are not altogether different, since the tropical abscess may be double instead of single, and even when single, by infecting adjacent liver tissue may give rise to the development of many secondary abscesses, and a number of small abscesses by peripheral extension may coalesce and give rise to a large single abscess.

Etiology.—Abscess of the liver is always the consequence of infection; the agents are various, and reach the liver by one of several pathways. The causative organisms are *staphylococci* and *streptococci*, *Entamœba histolytica*, *Bacillus coli*, *Bacillus pyogenes fœtidus*, *Bacillus typhosus*, *Bacillus dysenteriæ*, *Bacillus pyocyaneus*, *Diplococcus pneumoniæ*, *Proteus vulgaris*, *Actinomyces bovis*, etc. The infecting agent or agents may reach the liver directly, as when in consequence (1) of traumatism bacteria are introduced directly into the liver, or (2) when they reach the liver by extension of disease of adjacent organs; or the infection may be carried by the blood stream, that is, (3) by the portal vein, (4) by the hepatic artery, (5) by the hepatic veins; (6) or by the biliary ducts, or (7) by the lymphatics. The abscesses that result from traumatism or the extension of disease of adjacent organs are sometimes spoken of as primary, whereas those that result from the transport of infection from distant parts are called secondary abscesses; this distinction cannot always be maintained.

1. *Traumatism* occasionally gives rise to abscess of the liver. The resulting abscess is usually single and small or moderate in size.

2. *Diseases of adjacent organs* rarely give rise to abscess of the liver, but occasionally an ulcerative or suppurative (usually calculous) cholecystitis may perforate into the adjacent hepatic tissue and set up suppuration; or after the formation of adhesions, a gastric or duodenal ulcer or an ulcerating gastric carcinoma may invade the liver tissue and induce suppuration therein. The abscess is usually single and small, but sometimes it attains considerable size.

3. *Infection by way of the portal vein* is the commonest cause. In the great majority of cases amœbic dysentery is antecedent and the resulting abscess is spoken of as the single, tropical, or amœbic abscess.

The most common cause of this form of liver suppuration in temperate climates is *appendicitis*. In this the portal vein and its branches may or may not reveal thrombophlebitis, and the infection of the liver may result from extension of the thrombophlebitis, from metastases by way of the portal vein from the local disease in and about the appendix (the most common mode), or from transit of the infection through the retrocecal tissues to the liver. Other gastro-intestinal disorders also occasionally engender abscess of the liver, such as gastric and duodenal ulcers (transport of infection by the portal vein in the absence of adhesions), pyococcic, typhoid, tuberculous, actinomycotic, and neoplastic ulcers of the small and large intestine and the rectum, suppurative lesions of the pelvic organs (male and female), hemorrhoids, and infected thrombi following operations upon the intestine, rectum, anus, etc.

A solitary abscess of the liver may be a *hydatid cyst*, in which secondary infection has occurred.

4. *Infection by way of the hepatic artery* is rather uncommon and gives rise to small multiple so-called septicopyemic abscesses. These occur in pyococcic infections, especially infective endocarditis, purulent and fetid bronchitis, bronchiectasis, abscess and gangrene of the lungs, purulent pleuritis, suppurative periostitis, suppurative otitis media, infected operative or non-operative wounds, etc.

5. *Infection by way of the hepatic veins* may occur under exceptional circumstances, in which emboli may drop from the superior vena cava through the right auricle into the inferior vena cava and the hepatic veins. Perhaps it occurs also in other cases in which pyogenic bacteria from a suppurative focus in the pelvis or lower extremities, coming up the ascending vena cava, are forced into the hepatic veins by some violent motion and by a retrograde process infect the liver. This is most likely to occur with myocardial weakness and venous congestion.

6. *Infection by way of the biliary ducts* gives rise to abscess formation in the liver and in one of three ways: (1) By direct transport of the infection by way of the biliary passages themselves, such as may occur in infectious or suppurative cholangitis and pericholangitis, with extension to the adjacent interlobular tissues and the formation of multiple small abscesses; (2) by the extension of the infection in the biliary passages through the biliary mucosa to the subjacent vessels, thence to the portal vein (into which they empty), and the production of suppurative pyle-

phlebitis, in which event the process is analogous to that described in connection with infection by way of the portal vein; and (3) by direct extension of ulcerative and suppurative processes in the biliary tract (usually calculous cholecystitis) to the adjacent liver tissue.

7. *Infection by way of the lymphatics* may cause abscess of the liver under circumstances analogous to those that occasion infection by way of the portal circulation. In some cases, doubtless, the portal vein becomes involved after the infection has first gained the regional lymphatics; in other cases in which liver abscess, especially suprahepatic abscess, follows peritoneal disorders, the infection has followed the pathway of the lymphatics which converge from the peritoneum to the upper surface of the liver; in some cases of amœbic abscess of the liver the amœbæ probably reach the liver by traversing the peritoneum.

Pathology.—Abscesses the result of traumatism and of ulcerative and suppurative processes in adjacent organs are usually single and small or moderate in size, although those due to disease of adjacent organs sometimes attain considerable, usually superficial, extent. Inasmuch as these abscesses usually are situated near and involve some one of the surfaces of the liver, there is commonly a more or less extensive perihepatitis, adhesions binding the liver to the diaphragm or the adjacent organs. In some cases the collection of pus is on rather than within the liver, and merits the designation suprahepatic or infrahepatic abscess. In the small multiple metastatic abscesses in general arterial pyemia (hepatic artery infection) or portal pyemia (portal vein infection), in retrograde emboli (hepatic vein infection), or suppurative cholangitis, the liver is usually enlarged, swollen, and opaque, and presents the ordinary evidence of parenchymatous degeneration or cloudy swelling.

Symptoms.—Attempts are sometimes made to distinguish acute, subacute, and chronic abscesses; the distinction, however, is quite artificial, since although acute, subacute, and chronic abscesses do occur, a chronic abscess may remain latent for a long time and reveal itself acutely in consequence of some accidental disorder, such as trauma, intercurrent disease, etc., and suppuration that began acutely may subside and become virtually a chronic abscess. The symptoms of suppurative hepatitis vary with the nature and seat of the antecedent disorder, the pathway of infection, and the nature and virulence of the infectious agent. Many cases, especially of so-called tropical abscess, are entirely latent; often they are not detected until they have lasted some time; they may constitute an unexpected finding at necropsy.

Traumatic abscess as well as abscess due to spread of disease from adjacent structures, usually manifests itself by pain in the region of the liver, aggravated by motion and pressure, and referred to the right shoulder; palpable and audible friction (attributable to local perihepatitis); perhaps jaundice due to compression of the biliary ducts; chills, fever, sweats, and leukocytosis; enlargement of the liver, usually irregular; and perhaps a fluctuating tumor. The sequence of these phenomena upon an obvious trauma, especially if the skin and subcutaneous tissues have been lacerated, gives to them peculiar diagnostic significance that can scarcely be misinterpreted; to these are sometimes added the dis-

charge of pus through the wound, whereupon one has only to decide whether the abscess is about or involves the liver tissue. The detection of hepatic cells in the pus or in scrapings from the base of the abscess cavity settles the diagnosis, which, however, is usually a matter of academic interest, since the treatment cannot be other than surgical.

Multiple septicopyemic abscesses, whether due to portal vein, hepatic artery, hepatic vein, or biliary duct infection, often are not diagnosed; in perhaps the majority of cases their existence can be suspected only; that is, the symptoms of the primary disorder overshadow those due to the infection of the liver. In the one case the symptoms are those of a primary suppurative process in the heart (ulcerative endocarditis, purulent pericarditis), in another case in the lungs (abscess of lung or empyema); again, in the abdominal or pelvic viscera or in the extremities. The primary local process may be more or less obvious, and the general symptoms, chills, fever, sweats, and leukocytosis, are usually referred thereto; pain in the region of the liver may be inconspicuous or misinterpreted; the liver may not be noticeably enlarged (since death usually ensues early); pain in the shoulder may be interpreted as due to arthritis. In many cases the diagnosis of the liver involvement is of academic rather than of practical importance, since the condition is one of general septicopyemia, of which the hepatic involvement may be only a minor part; and its detection would not notably influence either the diagnosis or the treatment, although it might add materially to the seriousness of the prognosis. In some cases, however, particularly of so-called portal pyemia, but also of general arterial pyemia, or of spread of infection to the liver from suppurative cholangitis, the diagnosis is possible from a knowledge of the primary disorder and the development of local symptoms referable to the liver, the onset of which may be manifest by an aggravation of the general symptoms, especially the fever, sweating, and leukocytosis (or the marked decrease of a previous well-marked leukocytosis, significant of lessening general resistance). The significant local symptoms consist of pain in the region of the liver referred to the right shoulder, tenderness about the liver, perhaps a mild grade of jaundice, and enlargement of the liver. The enlargement may be quite regular, but the organ is likely to be softer rather than harder than normal; sometimes the enlargement is irregular and nodular, and the nodules may be soft or semifluctuating; in this event audible or palpable friction (perihepatitis) may be detected.

The so-called tropical abscesses and other liver abscesses of *intestinal origin* and slow (or comparatively slow) development are, as a rule, much more readily diagnosed; but some are so indefinite in their manifestations as to escape detection. Generally the onset is slow and insidious; sometimes for weeks or months the patient may complain of general ill-health; malaise, or gradually increasing weakness—which are especially significant if they constitute part of the poor health or delayed convalescence from dysentery and other intestinal disorders attended by suppuration or ulceration (such as appendicitis, etc.). In some cases the onset is sudden, attended by a chill or chilliness, and follows directly upon these intestinal diseases; in other cases, although

the noteworthy symptoms develop acutely, the antecedent disorder was present at some more or less remote time, and the abscess, doubtless previously latent, has been awakened into activity by some accidental cause. In another series of cases there have been one or several, sometimes recurring, attacks of what one may interpret as acute congestion of the liver, or acute hepatitis, especially in the tropics.

Suppuration of the liver is sometimes first suggested by *pain*, but one must remember that even a very large abscess may be altogether unattended by pain. In some cases early in the disease the pain is like that already mentioned in connection with active congestion or acute non-suppurative inflammation of the liver (due to tension of the capsule), which in reality usually precede the abscess formation. Pain when present varies with the situation of the abscess; when situated deep within the liver there may be no pain whatever, since the liver parenchyma is insensible to pain; the nearer the surface and the more marked the involvement of the liver capsule the more marked the pain; it may be acute, or merely a sense of weight or discomfort that may be increased by motion. With the progress of the abscess formation deep within the liver substance, the initial pain, that due to tension on the liver capsule, may entirely disappear (often occasioning an unwarranted sense of satisfaction); and it reappears when the abscess has reached the surface and provoked a perihepatitis, in which event the pain may be quite like that of pleuritis. The pain is not infrequently referred to the right shoulder, especially below the acromion process of the scapula, where it is usually dull and aching; this is said to be most common when the abscess is in the right lobe of the liver (the great majority of cases); occasionally it is referred to the left shoulder (abscess in the left lobe, in some cases at least); rarely it is bilateral. This pain also is due to the perihepatitis, which irritates the phrenic nerve which communicates with the superficial cervical plexus; the pain, therefore, is not significant of suppuration as such.

Jaundice is present in about 16 per cent. of the cases (58 of 375 cases, Thierfelder); usually it is slight, rarely marked. It is due to pressure of the abscess on adjacent biliary ducts or to cholangitis.

Constitutional symptoms, especially chills, fever, and sweating are of importance. A chill is not uncommon at the onset and a chill or chilliness, especially toward evening with a rise in the temperature, is rather frequent; but in some cases that develop slowly and become well encapsulated a chill may be missed—entirely or until late in the course. Fever is extremely important and probably essential to the diagnosis. It varies much in different cases. In perhaps the majority the elevation is in the evening, but the fever may be more or less continuous (especially early), remittent, or intermittent; sometimes the diurnal fluctuations are quite marked—96° to 104° or 105° F. In chronic and well-encapsulated cases the fever range may be slight; sometimes there is apparently no fever at all or only slight and transitory attacks; rarely the temperature is subnormal. Sweating is a common, almost a constant symptom; it is usually most marked at night, but may occur irregularly during the day, especially if the patient sleeps. Often the sweats are very profuse, and give

rise to great debility. The skin is frequently moist and clammy, especially upon the slightest exertion. Other manifestations are arthritic pains and sometimes swelling of the joints, and certain nervous symptoms, such as headache, insomnia, irritability, depression, etc.

Examination often discloses a general and facial aspect, the hepatic facies, readily recognized and of much diagnostic significance. The patient obviously is sick; the facial aspect is one of anxiety, distress, and more or less suffering; the complexion is muddy or sallow, or slightly icteric; the general integument is now hot and dry, now cold and moist; loss of flesh is progressive and is more marked the more severe and the longer the duration of the disease.

The *liver* is usually enlarged, although in some cases when the abscess is deeply seated and small, and sometimes even when it is quite large, no very noteworthy enlargement may be detected. The situation and direction of the enlargement depend upon the situation and direction of the abscess; since this is usually in the right lobe, the enlargement is usually in the right hypochondrium. In the early stages, when the abscess is still within the substance of the liver the enlargement is usually tolerably uniform; but as the abscess increases in size it commonly causes disproportionate enlargement of the liver upward and a corresponding change in the hepatic dulness; this often assumes a characteristic dome shape; that is, the upper limit of hepatic dulness rises near the mammillary line, reaches its highest point near the midaxillary line (where it may be on a level with the fourth or the third rib), and then descends, so that in the midscapular line it may be as low as the angle of the scapula. A decline of the upper limit of hepatic dulness near the vertebræ is quite characteristic of liver abscess. In some cases these changes are not present, as when the abscess occupies the left lobe, or when the enlargement of the liver is lateral rather than upward, or downward and anterior; in the last there may be bulging beneath the margin of the ribs or in the epigastrium, where on palpation one may detect a rounded or globular, smooth, and tense or semifluctuating tumor (depending upon whether the abscess actually projects beyond the surface or is still within the substance of the liver). In some cases definite fluctuation may be elicited. When enlargement cannot be made out by the usual methods, recourse may be had to the roentgen-rays, which disclose any irregular enlargement as well as the usual limitation of the movement of the diaphragm.

As the abscess approaches or reaches the surface of the liver perihepatitis is set up and friction may be detected; this suggests the point of election in the event of resorting to exploratory puncture. The muscles of the right upper quadrant of the abdomen become tense and there is usually considerable local tenderness. In some cases also there is local œdema, confined to one or two intercostal spaces or involving almost if not quite all the surface projection of the liver.

The urine is concentrated, of high color, increased specific gravity, and deposits an abundant sediment of urates and uric acid; as a rule, the amount of urea is diminished, but this is quite variable, although it is likely to be lessened if there is much destruction of the liver tissue;

indican, a small amount of albumin and albumose are sometimes present. Examination of the blood may reveal leukocytosis—a total count of 25,000 or more—and a relative increase of the polynuclear neutrophiles; unfortunately leukocytosis is not always found; it is likely to be absent in slow-growing, chronic, and well-encapsulated abscesses.

There are a number of other signs and symptoms that occur in varying combinations in different cases and are due to variable conditions. Thus, certain gastro-intestinal symptoms may develop, such as nausea and vomiting, which are most common when the left lobe is involved (local adhesions or pressure on the pylorus or duodenum); the appetite is usually poor, and the tongue coated in the centre, or smooth, red, and fissured; there may be constipation (usually when the abscess is latent) or diarrhœa (when there is marked congestion of the liver or in the acute hepatitis of the tropics); sometimes a latent dysentery is reactivated; and large amounts of pus may appear in the stools if the abscess ruptures into the bowel. Amœbæ may be found in the stools, especially if there is diarrhœa. The growth of the abscess upward, together with restricted movement of the base of the right chest and of the diaphragm, cause more or less congestion and compression of the base of the right lung, and lead to cough, dyspnœa, impaired percussion resonance, feeble or broncho-vesicular breath sounds, and fine rales; later, pneumonia may develop. In some cases a short, hacking, spasmodic cough ensues; it is usually referable to irritation of the diaphragm or an actual pleuritis, which in turn may have been due to transport of infection through the diaphragm or to rupture of the liver abscess into the pleura. The cardiac action may be embarrassed by the pressure of a large abscess, and the pulse rapid and irregular. The spleen usually is not enlarged and not palpable. Ascites does not occur unless there is some causative complication.

Spontaneous *rupture* is a common event in the course of large, especially tropical, abscesses of the liver. In Cyr's[1] series of 563 cases, rupture occurred in 159 (28.2 per cent.), as follows: Into the lung in 59, the pleura in 31, the pericardium in 1, the peritoneum in 39, the intestines in 13, the stomach in 8, the kidney in 2, etc. In Thierfelder's[2] collection of 170 cases perforation occurred into the lung in 74, the pleura in 26, the pericardium in 4, the intestines in 32, the peritoneum in 23, the stomach in 13, the kidney in 1, etc.

In a majority of the cases rupture occurs upward through the diaphragm (57 per cent. of Cyr's cases, 59 per cent. of Thierfelder's cases). In some cases purulent pleuritis results and gives rise to the usual signs thereof; in other cases (hepatopulmonary abscess) the pus finds its way into the lung either directly, in consequence of the early formation of adhesions (which is the rule), or indirectly, following a purulent pleuritis. When rupture occurs into the lung and the process finally involves and perforates a bronchus, a large amount of pus (perhaps mixed with blood) may be suddenly coughed up, or it may come up with very little effort, being evidently discharged in consequence of the release of the tension

[1] *Traité pratique des maladies du foie*, 1887.
[2] *Cyclopœdia of the Practice of Medicine*, v. Ziemssen, 1880, **9**, 138.

of the abscess; so great may be the amount of pus thus released that the patient's lungs may be inundated and sudden death may ensue. In other cases smaller amounts of pus are coughed up from time to time, but the total amount in the twenty-four hours may be considerable—10 to 12 ounces or more. The expectorated pus may exhibit ordinary purulent characteristics and contain necrotic liver tissue; usually, however, in the early stages at least, there is more or less blood mixed with the pus. Amœbæ may be found in it, should they be the exciting cause. Should the condition progress favorably, which it does in many cases, the amount of pus expectorated gradually diminishes and ultimately ceases, and the patient recovers. In other cases the expectoration lessens or ceases, but the patient's general condition becomes worse, and chills, fever, and sweats recur; evidently drainage has become insufficient and pus accumulates. Again, a large amount of pus may be discharged, and again the expectoration may cease; such variation may recur for some time until recovery ensues or the patient dies. A second unruptured abscess should be suspected in the event of persistence of the septic phenomena, despite evident free drainage.

Rupture into the stomach or the duodenum is usually followed by epigastric distress, nausea, vomiting of considerable pus, diminution in the size of the liver, and perhaps relief of the local symptoms referable to the liver. Rupture into the intestine is followed by diarrhœa and pus in the stools; the pus frequently is overlooked, especially when the rupture occurs into the small intestine. Perforation into the peritoneum may occur into preformed adhesions, whence a localized extrahepatic abscess may ensue, or into the general peritoneal cavity, in which event a generalized peritonitis may be set up; but sometimes, in view of the fact that the abscess may be sterile, peritonitis may not immediately ensue and the patient, if operated upon, may recover.

Diagnosis.—This is often attended with considerable difficulty. The most suggestive signs are the etiological factors, which vary with the source of infection, but which should be carefully studied; pain in the region of the liver, perhaps referred to the right shoulder; progressive enlargement and tenderness of the liver; slight jaundice, and chills, fever, sweats, and leukocytosis. These symptoms, however, are not always outspoken; the leukocytosis, for instance, may be slight, and the so-called tropical abscess may be latent for a long time, and when somewhat active may give rise to quite indefinite symptoms.

Manson[1] states: "Golden rules in tropical practice are to think of hepatic abscess in all cases of progressive deterioration of health; and to suspect liver abscess in all obscure abdominal cases associated with evening rise of temperature, and this particularly if there be enlargement of or pain in the liver, leukocytosis, and a history of dysentery—not necessarily recent dysentery. If doubt exists, there should be no hesitation in having early recourse to the aspirator to clear up the diagnosis." "The most common mistakes in diagnosis are: (1) Failure to recognize the presence of disease of any description, even when an enormous

[1] *Tropical Diseases*, 1907, 4th edition, 510.

abscess may occupy the liver. (2) Misinterpretation of the significance and nature of a basic pneumonia—a condition so often accompanying suppurative hepatitis. (3) Attributing the fever symptomatic of liver abscess to malaria. (4) Mistaking other diseases for abscess of the liver, and *vice versa*—for example, hepatitis of a non-suppurative nature; suppurative hepatitis before the formation of abscesses; syphilitic disease of the liver—softening gummata which are often attended with fever of hectic type; pylephlebitis; suppurating hydatid; gall-stone and inflammation of the gall-bladder, subphrenic abscess; abscess of the abdominal or thoracic wall; pleurisy; encysted empyema; pyelitis of the right kidney; pernicious anemia; leukemia; scurvy and similar blood diseases associated with enlargement of the liver; ulcerative endocarditis; kala-azar; Malta fever; trypanosomiasis. Any of these may be attended with fever of hectic type, increased area of hepatic percussion dulness, and pain in and about the liver."

Malaria may be excluded by disproportionate enlargement of the liver as compared with the spleen (the reverse being the case in malaria); absence of malarial parasites in the blood; polynuclear leukocytosis; and the non-response to quinine. Cholelithiasis and Charcot's biliary intermittent fever may be excluded by the absence of a history of cholecystitis, cholelithiasis, and biliary infection; the absence of attacks of fever, etc., separated by longer or shorter periods of apyrexia; non-occurrence of increase in the jaundice after each attack; and the absence of serious impairment of the general health.

Prognosis.—The small multiple abscesses of the liver are almost invariably fatal, death usually resulting within one to three weeks. Many of the large single so-called tropical abscesses eventuate in recovery; their duration, however, is uncertain, since it is not possible always to say when they began; they are often latent for a long time. The outlook after rupture into the lung and evacuation through a bronchus is rather favorable (75 per cent. of recoveries, De Castro), although the condition may last for months; rupture into the hollow abdominal viscera or externally may also be followed by recovery; but rupture into the peritoneum, the pericardium, etc., is usually fatal. Recurrence of the abscess may follow apparent recovery.

Treatment.—This is essentially surgical in such forms as are amenable to treatment. The treatment of the multiple septicopyemic abscesses is that of septicopyemia in general. Rogers has claimed remarkable results in amœbic abscess by the use of emetin. Several authors advocate the use of ipecac, instead of emetin, on the ground that the latter tends to drive the entamœbæ into the encysted or latent stage, whence relapses are bound to recur (Simon).

The diagnosis of the large single abscess furnishes the indication for its evacuation; and even when the diagnosis of a single abscess cannot be made positively, although hepatic suppuration is obviously present, resort should be had to operation. In the event of perforation of the abscess, immediate operation is indicated; operation is indicated also in the event of perforation into the lung, hollow abdominal viscera, etc., but it need not be undertaken immediately, since in many of these cases

spontaneous recovery ensues; signs warranting delay consist of good general condition of the patient, minor septic or toxic phenomena, free discharge of pus, improvement in the local conditions, etc.

In suppurative hepatitis, due to infection with pyogenic cocci, or *Bacillus typhosus*, *Bacillus coli*, etc., intravenous use of mercurochrome in dosage of 5 mg. per kilo of body weight[1] might be worth a trial, as the excretion of mercurochrome is in large part by way of the liver.

CHRONIC INTERSTITIAL HEPATITIS: THE CIRRHOSES OF THE LIVER

Chronic interstitial hepatitis, comprising the so-called cirrhoses of the liver, has been much and variously classified—etiologically, anatomically, and clinically.[2] The disorder was first described by Vesalius, but the term cirrhosis was first employed by Laennec to describe the yellowish "hobnails," which he regarded as new growth.

Eliminating from consideration cases of: (1) So-called capsular cirrhosis (more properly called perihepatitis or hepatic capsulitis), in which the liver tissue may not be at all affected, except perhaps secondarily from compression or by slight ingrowth of new connective tissue from the capsule; (2) so-called cardiac cirrhosis or cardiac liver, (3) syphilis of the liver; and (4) circumscribed or focal fibroses which follow limited inflammatory and degenerative processes, focal necroses, chronic obstruction of the biliary ducts (pericholangitis), etc., there are two types of chronic diffuse disorder of the liver, attended by fibrosis, to which the term cirrhosis may be limited. One of these disorders is very common; it is usually due to the misuse of alcohol; it is characterized by moderate enlargement of the liver (which in advanced stages may become reduced in size), by phenomena of portal obstruction (notably hematemesis and ascites), and by the absence or unimportance of jaundice; and after the development of symptoms it usually runs a comparatively short course (Laennec's portal, alcoholic, or multilobular cirrhosis). The second of these disorders is rare; it is of unknown etiology; it is characterized by marked and persistent enlargement of the liver and spleen, by chronic jaundice, by periodic attacks of abdominal pain and fever, and by the absence of manifestations of portal obstruction (notably ascites); and it runs a comparatively long course (Hanot's, biliary, or monolobular cirrhosis).

There can be no serious objection to the use of the terms Laennec's and Hanot's cirrhosis, aside from that inherent in eponymic terms. Alcoholic cirrhosis accurately describes most, but not all, cases of Laennec's cirrhosis; but alcohol perhaps sometimes gives rise also to Hanot's cirrhosis, although this is a disputed point, and the study of the etiological factors is important from many points of view, particularly the therapeutic. The terms atrophic and hypertrophic, to designate, respectively, a small and a large liver, are most ill-advised and have led to confusion and misapprehension. There has been much discussion as to whether or not there is a so-called hypertrophic stage of atrophic

[1] Young, Hill, and Scott: *Arch. Surg.*, 1925, **10**, 813.
[2] Consult Epplen: *Arch. Int. Med.*, 1922, **29**, 482.

or Laennec's cirrhosis, and this so-called hypertrophic stage has been confounded with what is spoken of as hypertrophic or Hanot's cirrhosis. Aside from notable variations in size that may occur within a comparatively short time in a liver the seat of Laennec's cirrhosis, a small or so-called atrophic liver is often hyperplastic to a considerable degree, and a large or so-called hypertrophic liver always exhibits considerable atrophy of the hepatic parenchyma; and many cases of Laennec's cirrhosis result fatally while the liver is still larger than normal; that is, in many cases the so-called atrophic liver does not become atrophic (smaller than normal), but remains to the end, as it were, hypertrophic. The terms assuredly are inadequate to describe the conditions, and should be discontinued.

The preferable terms for the two main types of cirrhosis, of which there are subtypes, are portal and biliary; portal, because the etiological factor is perhaps always transmitted by the portal circulation, the new-formed connective tissue is specially conspicuous in and about the portal spaces in the liver, and the obtrusive symptoms are those of portal obstruction; biliary cirrhosis, because the essential lesion is a radicular cholangitis and the conspicuous clinical feature is jaundice, due to obstruction to the free flow of bile.

Two subtypes of biliary cirrhosis are sometimes differentiated: (1) The hypertrophic biliary cirrhosis of Hanot; and (2) an obstructive biliary cirrhosis—by which is meant a condition of pericholangitic fibrosis spreading to the adjacent liver lobules in obstruction of the extrahepatic biliary ducts. The disorder was first described by Wickham Legg, and later by Charcot and Gombault, Gilbert and Sourmont, Chauffard, Ford,[1] Weber,[2] etc. There is no doubt that fibrosis does occur in the liver in some cases of chronic obstruction of the extrahepatic biliary ducts; but the fibrosis is usually minor in grade, develops about the intrahepatic biliary ducts (pericholangitis), seldom implicates the liver lobules to a noteworthy degree, and of itself does not give rise to noteworthy symptoms; the symptoms remain those of the obstruction (especially chronic jaundice and acholic stools), to which subsequently may be added phenomena attributable to disorganization of the hepatic parenchyma. Compression of the common bile duct, with complete interruption to the flow of bile is often attended by serious consequences, such as dilatation of the intrahepatic ducts with rupture of the biliary capillaries leading to degeneration and necrosis in the centre of the lobule, or to compression atrophy, degeneration, and pigmentation of the liver cells; in some cases also some replacement fibrosis occurs, but in degree it is by no means comparable to that of cirrhosis in the ordinary sense. The inference is that in most cases of considerable fibrosis of the liver in chronic obstruction of the biliary ducts, factors other than the obstruction are the real cause of the fibrosis. In some cases this is doubtless infection of the biliary tract, with connective cholangitis and pericholangitis, as occurs in some cases of cholelithiasis, with more or less incomplete obstruction; in other cases, the common causes of portal cirrhosis, The proper inter-

[1] *Am. Jour. Med. Sci.*, 1901, **121**, 60.
[2] *Trans. Path. Soc.*, Lond., 1903, **54**, 103.

pretation of the phenomena is of importance and interest; those who interpret localized fibrosis as cirrhosis will continue to speak of the condition as obstructive biliary cirrhosis; but it is not beyond the facts to assert that biliary obstruction of itself does not give rise to cirrhosis in an acceptable sense, that the fibrosis that does occur is not of constant type, is almost negligible anatomically, and is assuredly negligible clinically, and that when a noteworthy cirrhosis occurs in association with obstruction to the biliary ducts it is probably due to the ordinary causes of cirrhosis rather than to the obstruction.

Portal Cirrhosis. — Portal cirrhosis is a chronic degenerative and inflammatory disease of the liver characterized by recurring degeneration and regeneration of the hepatic parenchyma and by fibrosis in and about the interlobular or portal spaces, all of which leads ultimately to obstruction of the portal circulation.

Etiology.—Portal cirrhosis is peculiarly a disease of adult life; it is most common during the fifth decade, the majority of the subjects succumbing before the fiftieth year, forty-eight and seven-tenths years being the average age of 121 males, and forty-seven years of 44 females, (Rolleston). It is, however, by no means rare at the extremes of life. A notable number of cases occur in young children, in whom it is often fatal before the sixth year. It is a little more than twice as common in men as in women; and it is also more commonly latent in men. Occupation is of significance only as it concerns other factors, notably alcoholism.

Portal cirrhosis is undoubtedly the expression of the activity of some poison or poisons; these are various in nature, and may reach the liver by way of the portal vein, the hepatic artery, or both. In the great majority of cases the portal vein is unquestionably the pathway. From time immemorial major importance has been attributed to alcohol, and assuredly with reason; but during recent years attempts have been made to minimize its influence, and its action is probably indirect rather than direct. Alcohol is especially active when taken in the form of distilled liquors, but cirrhosis occurs also in those addicted to the use of wine, beer, ale, porter, etc., and it is more common among those who drink constantly a small amount than among those who occasionally drink a considerable amount. The stronger liquors are the more active probably because they are often taken on an empty stomach and consequently reach the liver in concentrated form. How the alcohol acts is not definitely known, but it is likely that it acts: (1) As a direct irritant or poison to the liver cells (of which there is sufficient experimental proof), causing parenchymatous and fatty degeneration, even necrosis, or disturbing the functions of the liver cells and rendering them unduly susceptible to the influence of other causative factors (autogenic poisons, bacterial toxins, etc.), as well as irritating the connective tissue of the organ; and (2) by causing gastro-intestinal catarrh and thus favoring the formation of toxins inseparable from that condition which, transported by the portal vein, may be the active factor in provoking cirrhosis in a liver otherwise rendered vulnerable. It has been suggested that ethyl alcohol is not the active factor but rather adulterants, such as

amyl alcohol, the aldehydes, etc.; but this is pure hypothesis. Cirrhosis occurs in the absence of alcoholism and not all alcoholics become cirrhotic. In cases in which alcohol seems to be, or is, the only obviously active factor, there may be a lowered vitality on the part of the liver that renders it especially susceptible; and this is doubtless true also in respect to other etiological factors.[1] That hereditary influence is sometimes operative is suggested by the occasional occurrence of several cases of cirrhosis in one family; but one cannot overlook the likelihood of familial addiction to alcoholism as well as congenital syphilis.

There is reason to believe that poisons, particularly the fatty acids (lactic, butyric, acetic, valerianic, etc.) and other ill-understood enterogenic toxins may be causative factors, especially in non-alcoholic subjects who give a history of overindulgence in highly seasoned foods, spices, etc. (dyspeptic cirrhosis, Budd's non-alcoholic cirrhosis). The fatty acids and other toxins rarely may be ingested with the food; but they are much more likely to be manufactured in the intestinal tract in cases of gastrointestinal catarrh; experimentally lesions resembling those of cirrhosis have been produced by injecting fatty acids into lower animals. To the influence of enterogenic toxins, spices, etc., may also be attributed the cirrhosis occurring among the Hindus, Egyptians, etc., who, avoiding alcohol, nevertheless often eat food that is not above reproach and are quite partial to condiments and spices. It is possible that a poison elaborated in the spleen may cause cirrhosis in splenic anemia.

Infections of various kinds may be followed by cirrhosis, but the relationship of the one to the other has not been determined. In most of these cases the infection is carried to the liver by the general as well as by the portal circulation. Many acute infections cause pathological changes in the liver and some of these are followed by fibrosis—usually localized and minor or moderate in grade; but this scarcely constitutes cirrhosis. McCrae and Klotz[2] believe that the focal necroses in typhoid fever are caused by toxins and that they do not contain bacteria. These changes may perhaps lead later to cirrhosis. A malarial cirrhosis has been widely commented upon, but it is probably not as common as many observers believe: both diseases may occur concurrently. Tuberculosis is sometimes associated with cirrhosis, especially fatty cirrhosis, and some observers believe that the tubercle bacillus or its toxin may set up the lesions of cirrhosis. The lesions in the liver caused by syphilis are not those of cirrhosis (in a restricted sense), but antecedent syphilis may render a liver unusually susceptible to the ordinary cause of cirrhosis. A form of cirrhosis in Egypt and elsewhere has been attributed to a toxin elaborated by *Uncinaria duodenalis* and *Bilharzia hæmatobia*. Rogers[3] described a peculiar form of intralobular cirrhosis produced by the parasite of kala-azar. Adami's observations relating to a so-called diplo-

[1] Consult Kern's article on changes in the liver in chronic alcoholism (*Ztschr. f. Hyg. u. Infectionskrank.*, Leipz., 1912, **73**, 143) and Mathias Thiesen on Atrophic (Laennec's) Cirrhosis of the Liver (*Dissert., Strassburg*, 1912). Both these articles contain interesting statistics gathered from a wealth of autopsy material upon the subject of the influence of alcohol on the liver.

[2] *Jour. Path. and Bacteriol.*, Cambridge, 1908, **12**, 279.

[3] *Ann. Trop. Med. and Parasitol.*, Liverpool, July, 1908.

coccic form of the colon bacillus in cirrhosis in man and in infective cirrhosis in cattle is of interest, not so much as suggesting an etiological relationship, but as illustrating the bactericidal properties of the liver cells. Bacteria may be indirectly the cause of cirrhosis by setting up processes in the intestine, the toxins of which, transported to the liver, may act as the direct irritant factor.

Other sorts of irritants sometimes appear to give rise to cirrhosis. Thus in hemochromatosis, in consequence of hemolysis, blood pigment is set free and infiltrates the tissues, and the liver and the pancreas become fibrotic. Cirrhosis of the liver has been found in association with pneumonokoniosis, and in poisoning with lead, silver, arsenic, etc.

Experimentally, so-called cirrhosis, but usually minor and circumscribed fibrosis, has been produced by injecting certain bacteria, alcohol, and other irritants, such as chemicals, vegetable alkaloids, etc., into the portal circulation, the general circulation, and the intestine. Much more significant are Pearce's[1] studies regarding the effects of hemolytic and hemagglutinative sera; the early necrotic lesions in the liver are followed by reparative processes that constitute a chronic interstitial hepatitis; these demonstrate that cirrhosis may follow widespread destruction of necrotic lesions in the liver, and explain the histogenesis of cirrhosis and other reparative processes in the liver. Opie[2] demonstrated that cirrhosis of the liver can be experimentally produced by administering chloroform by mouth and injecting bacteria into the blood.

Pathology.—The liver varies much in size in different cases, and in the same case at different times. At the necropsy it may be very small, weighing only 970 gm. or less; or it may be very large, weighing as much as 4000 gm. or more; but in the majority of cases at autopsy it weighs more than normally. Rolleston states that the average weight of the liver in 155 consecutive necropsies on cirrhotic subjects at St. George's Hospital was 63.6 ounces (1978 gm.): the average weight of the liver in 100 cases collected by Hawkins was 52 ounces (1617 gm.), the minimum being 32 ounces (995 gm.), and the maximum 74 ounces (2300 gm.); and the average weight in 93 cases collected by Kelynack was 53 ounces (1648 gm.). In fatal cases in young subjects the liver is relatively and often absolutely larger than in older subjects.

Variations in the size may be due to different factors. It is essential to bear in mind that in the usual course of events the liver may be enlarged from the beginning to the end of the disease. It is often said that the liver is enlarged in the early stages and small in the later stages —in consequence of contraction of the newly formed fibrous tissue. This change in size is sometimes observed, but it is incorrect to assume that the decrease in size is due always or solely to contraction of the new fibrous tissue. Marked variations in size often occur rapidly, within several days or weeks, and are due solely to changes in the vascular supply. A liver small at one examination may be much enlarged subsequently. The large liver may be due to vascular engorgement, hyperplasia of the liver cells, disproportionate fibrosis that is likely to be diffuse, as in the so-called monolobular type, and fatty cirrhosis.

[1] *Jour. Exper. Med.*, 1906, **8**, 64; *Jour. Med. Research*, 1906, **15**, 99 (literature).
[2] *Jour. Exper. Med.*, 1910, **12**, 367.

As a rule, the liver is of increased density (increased specific gravity), so that a small liver may weigh more than a liver of normal size; it is of increased consistency and lessened elasticity. The capsule is often opaque, sometimes considerably thickened, and not infrequently adherent to the under surface of the diaphragm. Adhesions, when present, are usually old, fibrous, and circumscribed rather than widespread; occasionally, however, they are almost if not quite universal and may extend to adjacent organs—the gall-bladder, stomach, intestine, omentum, through the diaphragm to the pleura, lung, etc. In other cases more or less recent, acute, fibrinous adhesions are encountered.

The *surface* of the liver is distinctly granular, the small livers more so than the larger ones: grayish-white opaque depressions alternate with pale, yellowish-brown, sometimes reddish-brown, roundish or ovoid elevations—the so-called granular or "hobnail" liver. The hobnails vary considerably in size, from those scarcely larger than a pinhead (under which circumstances the surface of the liver is comparatively smooth) to others 1 to 2 cm. in diameter; usually they average from 2 to 4 mm. in diameter. Sometimes many—ten or more—hobnails appear specially surrounded by an unusually wide band of connective tissue that isolates them from adjacent tissue and causes a more marked projection. These lesions usually are distributed uniformly throughout, but occasionally one lobe is more involved than the others; the left lobe especially may be very small (lessened resistance? influence of splenic blood?); rarely the caudate, quadrate, or Spigelian lobe may be disproportionately affected.

On section the liver cuts with increased resistance, being much denser, firmer, and tougher than normally. The cut surface reveals interlacing bands of whitish or grayish-white fibrous connective tissue that vary somewhat in thickness, pervade the entire organ, and are continuous with the grayish opaque depressions on the surface. These bands, which obviously take their origin in the periportal spaces, form a network that encloses or surrounds islets of liver tissue that vary in size from that of a pin-point to others 1 cm. or more in diameter; the larger islets are made up of several, often eight, ten, or more, liver lobules (or remains of liver lobules), and are pervaded by more delicate bands of connective tissue (so-called multilobular cirrhosis). In many, but not all, cases the islets of liver cells appear to be under some tension, since on section they project somewhat; it is not improbable that this is due to the elastic tissue of which in part the newly formed connective tissue consists. The liver tissue is usually pale yellowish in color or yellowish brown; occasionally it is greenish (from staining with bile), or reddish or brownish, especially in the centres of the lobules (from staining with blood or blood pigment). The islets of liver tissue are sometimes very large, hyperplastic, evidently the result of active proliferation, a condition sometimes spoken of as nodular cirrhosis, or cirrhosis with multiple adenoma. This process, doubtless at first compensatory, sometimes becomes unrestrained and results in the production of carcinoma (cirrhosis with carcinoma). Occasionally the islets of liver tissue are very pale (fatty degeneration) and at first sight resemble new-growth; in some cases the centres of some of the nodules are quite soft and necrotic.

The bloodvessels show more or less well-marked changes. The hepatic artery and its smaller branches are often distended—doubtless related to the necessity of supplying with blood the increased fibrous tissue; in some cases the vessels exhibit the ordinary lesions of endarteritis, especially in the cirrhosis of hemochromatosis and of syphilis. The hepatic veins may show the lesions of obliterating endophlebitis, as has been pointed out by Hess.[1] The smaller intrahepatic branches of the portal vein, especially those between the liver lobules, are often compressed and not infrequently thrombosed; the larger intrahepatic branches, the main trunk, and the gastro-intestinal branches that go to form the main trunk are usually dilated; the wall of the vein is often thickened—periphlebitis and endophlebitis; and thrombosis of the main trunk may occur (more common in cirrhosis than in any other condition).

Communications between the portal vein and the systemic circulation constitute a part of the cirrhotic process. For the most part these consist of dilatations of normally existing anastomoses. They subserve the useful purpose of diverting to the superior and the inferior venæ cavæ the venous blood in the portal tributaries flowing against the obstruction in the portal distribution in the liver, and thus they relieve the portal congestion. Although usually present, they are not always observed; they are sometimes absent in fatal cases of cirrhosis in which death has resulted from other causes.[2] Through increased pressure in the portal circulation various anastomoses become dilated, thus giving passage to the venous blood obstructed by the cirrhotic liver. Various compensatory anastomoses occur. Rolleston considers them under the heading of (1) general and (2) local.

1. *General communications* between the retroperitoneal veins opening into the lumbar and azygos veins, and the veins of the peritoneum and of the intestines. Also branches of the portal vein anastomosing with the inferior vena cava, as described by Retzius, producing at times an intense injection of a large part of the parietal peritoneum.

2. *Local.*—Internal porto-caval anastomoses developing in the lobules of the liver between branches of the portal vein and the intralobular vein. Communications may develop between the veins in the substance and capsule of the liver and the phrenic and intercostal veins, where the liver and diaphragm are uncovered by peritoneum. In addition a large vein running to the umbilicus in the falciform ligament may communicate with the veins of the abdominal wall, thus connecting the portal vein with the deep epigastric and external iliac veins, producing a "Caput Medusæ" most marked around the umbilicus. The veins of the œsophagus, which open into the azygos veins, communicate at the cardiac orifice with the gastric veins and so with the portal vein. In this way œsophageal varices are formed from which hemorrhages may occur. In cases of ascites with obstruction of the inferior vena cava a "Caput Medusæ" also occurs, due to enlargement of the veins of the skin connecting with the superior and inferior epigastric veins. Here

[1] *Am. Jour. Med. Sci.*, 1905, **130**, 986.

[2] For an excellent study with a review of the literature consult also Gilbert and Villaret, *Rev. de med.*, Par., 1907, **27**, 305.

the dilated veins run from the middle of the groins to the costal arches and avoid the umbilicus.

These anastomoses serve both a useful and an evil purpose. On the one hand, as long as the collateral circulation is efficient, obstructive symptoms are in abeyance and the liver is enabled better to perform its functions, perhaps enabled to regenerate, whence in some cases the disease remains or becomes latent, even apparently cured; on the other hand (*a*) the dilated veins are likely to rupture, either spontaneously or in consequence of trauma, and lead to hemorrhage; and (*b*) much of the blood from the gastro-intestinal tract being thus diverted from the liver to the general circulation, conditions somewhat analogous to those induced by the establishment of an Eck fistula supervene, much of the products of digestion are not brought to the liver and toxemia ensues.

The gall-bladder and the biliary ducts are usually normal; occasionally there is some thickening of the wall of the gall-bladder from chronic cholecystitis. Calculi may be found in the gall-bladder or the ducts: in 21 (15.4 per cent.) of 136 fatal cases (Rolleston); in 18 (8.6 per cent.) of 209 men, and in 7 (17 per cent.) of 41 women (Klopstock).

Histology.—A clear conception of the cirrhotic process is best attained by bearing in mind that, as emphasized by Kretz,[1] the liver is not made up of acini in an acceptable sense. While the physiological unit is that collection of cells drained by a radicle of the bile duct, this unit is scarcely delimitable anatomically; nor are the so-called acini, or lobules, cross-sections of which, surrounded by connective tissues, form such a conspicuous feature of microscopic sections, of such simple structure as at first appears. Study of the liver in serial sections and its reconstruction show that the liver parenchyma does not form isolated acini, or lobules, everywhere surrounded by connective tissue, but that what appear to be acini are merely cross-sections of liver cells arranged as a mantle about the numerous dendritic ramifications of the hepatic vein, and that this mantle is nowhere discontinuous, forming, on the contrary, a continuous whole, everywhere connected, particularly at the points of junction of the sublobular, lobular, and lobar veins. The intimate relationship that the liver cells structurally bear to the hepatic vein is further shown by the radial disposition of the cells about the branches of this vein—the so-called central veins.

The liver has two sources of blood supply—the portal vein and the hepatic artery—which commingling form a plexiform capillary network, in the meshes of which the liver cells are arranged. Ultimately, the capillaries unite again to form the radicles of the hepatic vein, which empty into the so-called central veins. Opie[2] especially has directed attention to the fact that one of the important characteristics of the liver is its susceptibility to variations in blood-pressure, saying: "The portal vein, hepatic artery, and hepatic vein are in such free communication that the entire lobule can be injected from any one of these vessels. Hence artificial injections do not define the intralobular distribution of the portal

[1] Ueber Lebercirrhose, *Wien, klin. Wchnschr.*, 1900, **13**, 271; *Verhandl. d. deutsch. path. Gesellsch.*, Berl., 1904, **8**, 54; *Internat. Clin.*, Phila., 1905, **3**, 289.

[2] *Jour. Med. Research*, 1904, **12**, 147.

and arterial blood, for doubtless differences of venous and arterial pressure have a part in determining peculiarities of the circulation within the lobule." Opie's experimental studies led him to the conclusion "that both the hepatic artery and portal vein pour their blood into the periphery of the lobule, and here the influence of the arterial blood-pressure is most strongly felt. When foreign material reaches the liver by the portal vein it is washed from the peripheral zone by the arterial blood, and tends to be deposited in a middle zone, where the influence of the opposing circulation is less strongly felt. Hence it is not improbable that toxic substances capable of causing necrosis of the hepatic cells, brought to the liver by the portal vein, might first exert their effect upon cells within a mid-lobular zone. The periphery of the lobule, moreover, is supplied with arterial blood, and is perhaps for this reason less susceptible to injurious agencies."

In the parenchyma of the liver in a moderately advanced or well-advanced case of cirrhosis, certain deviations from the normal become apparent—changes in the size, shape, and configuration of the lobules, and in the arrangement of the liver cells; degenerative, atrophic, and hyperplastic changes in the liver cells; changes in the vascular arrangement and supply.

The size of the lobules or "hobnails" in cirrhosis has been studied by Kretz, MacCallum, etc. Kretz has shown that the normal lobules are roundish polygonal in shape, with their long axes in the direction of the central vein, and (as is well known) that their greatest diameter is usually a little more than 1.5 mm., and may reach 2.5 mm., whereas the short diameter is about 1 mm., and that in cirrhosis these figures are surpassed, some lobules being much larger, and other collections of cells much smaller. MacCallum found that while the average radius of a lobule (that is, the thickness of the mantle of cells about the central vein) in a number of normal livers is about 0.66 mm., in advanced cirrhosis lobules are encountered that measure, from central vein to periphery, 1 mm. or more, the small diameter, therefore, being more than 2 mm.

There is a notable departure from the normal shape and configuration of the lobules; many of them are no longer rounded, but quite irregular in transverse section; many of the cell mantles no longer surround the central veins equally on all sides, but very unequally, so that many central veins are situated eccentrically in a more or less misshapen lobule; many so-called lobules have no central vein at all (and are not tangential sections of otherwise normally arranged lobules); certain lobules (or so-called lobules, usually remains of several) have two, three, four, or more central veins; and often the central vein may be seen in the adjacent interlobular connective tissue. Thus the mantle of cells covering a central vein varies much in thickness in different regions (transverse planes), sometimes exposing, sometimes covering, the vein to a greater or less extent; and although isolated collections of liver cells (that is, collections devoid of central veins) do occur, some supposedly isolated collections are merely sections of more or less irregularly proliferating dendritic branches of what may be called the parent stem, or mantle covering a single central vein.[1]

[1] Consult Epplen: *Arch. Int. Med.*, 1922, **29**, 482.

Furthermore, although the normal radial arrangement of the liver cells about the central vein is preserved to some extent, in many places it is totally wanting; the architecture of the lobule has become altered so that the cells are arranged irregularly in parallel rows, etc. This is quite as well-marked in many of the lobules that have a central vein as in those collections of cells entirely devoid of central veins.

The parenchymatous cells show various degenerative changes. In the early stages many cells become degenerated, necrotic, and are removed, but from the nature and the stage of the process at which this occurs, it is rarely observed, except in cases that run a rapid course and in certain cases of pigmented cirrhosis. In some cases there is considerable or widespread fatty infiltration (so-called fatty cirrhosis). In advanced cases considerable atrophy of the liver cells may be observed.

Evidences of *hyperplasia* of the liver cells are readily found in almost every cirrhotic liver, even in far-advanced cases. Mitoses are rarely encountered in advanced cases—largely in consequence of the nature of the process, the advanced stage at which the examination is generally undertaken, and the length of time after death that the liver is obtained, time sufficient for the completion of any mitoses present at death. That many of the liver cells are newly formed is quite apparent from their large, clear, and plump appearance, their rounded (rather than polygonal) outline, the presence of two or more nuclei, and the absence of fat and of pigment from their protoplasm. These cells, sometimes small collections of them, are situated amidst other liver cells normal in size and outline, provided with only a single nucleus each (though sometimes with two nuclei, which is quite normal), and the protoplasm of which is normally pigmented and contains fat. It is probable that liver cells always regenerate from preëxisting liver cells. Necrotic and hyperplastic changes may be found in the one lobule.

A characteristic feature of almost all cases, more conspicuous in some cases than in others, is the bile-ducts or so-called pseudobiliary canaliculi, the nature and origin of which have occasioned much discussion. Doubtless the great increase of these structures in cirrhosis is relative only, and due in part, but only in small part, to mutual approximation of already existing bile ducts occurring in consequence of loss of the liver tissue; but that most of them are newly formed is generally conceded, and is quite apparent from their excessive number and the evidences of active proliferation (mitosis) that they commonly exhibit. Their origin has not been determined definitely for all cases. It seems quite certain that some, at least, result from proliferation of existing bile ducts; on the other hand, since they are found in a wide variety of disorders, such as all forms of cirrhosis, acute yellow atrophy, in the neighborhood of tubercles, gummas, etc., in other words, in diseases alike only in that they destroy liver tissue; since they differ from normal bile ducts in the absence or relative paucity of encircling elastic tissue; since they have been found to be directly continuous with liver cells; and since in cases in which the liver cells have been much destroyed they are found in large numbers in what may be interpreted as the remains of the skeleton of the lobule, we are quite warranted in the opinion that they may result from prolifera-

tion of the liver cells themselves, constituting a reversion to a less highly specialized type of structure. The important fact to point out is the histogenetic equivalence of the liver cells and the epithelium of the bile ducts, and the fact that proliferative changes of the liver parenchyma are a conspicuous feature of common cirrhosis.

The changes in the *connective tissue* vary with the stage and activity of the process. Early there is more or less round-cell infiltration in and about the portal spaces; later there is considerable increase in the amount of connective tissue—in part the result of organization of the inflammatory exudate, in part a replacement fibrosis to fill up potential lacunæ left by destroyed liver parenchyma. This newly formed connective tissue commonly encloses rather than invades the liver lobules; sometimes only one lobule is enclosed in a wide band of connective tissue, sometimes many lobules—whence the designation *multilobular* cirrhosis.

A conspicuous change is the great increase in the elastic tissue—probably more or less intimately related to the great increase in the capillaries derived from arterioles; this elastic tissue not only makes up a large part of the fibrous bands between the lobules, but it is also found to some extent within the lobules, and occasionally a very small amount of it is found about or in the immediate neighborhood of the central veins. A not inconsiderable part of the fibrosis is made up of reticulum—not only the reticulum normally between the lobules, but the intralobular reticulum—that remaining after the liver cells have degenerated and been removed.

Lesions in other Organs.—The *spleen* is enlarged in at least 80 per cent. of the cases (198 of 250 cases, Klopstock;) it is probably enlarged some time during the course of all cases, but variations in size are due to different factors. There is no constant relationship between the size of the liver and of the spleen. At the necropsy the average weight of the spleen is about 400 grams; the average weight of 32 cases at the Lankenau Hospital, Philadelphia, was 400 gm. the minimum 110 gm., and the maximum 1320 gm. In the early stages, in consequence of increased vascularity, proliferation of the splenic pulp, and hyperplasia of the endothelial cells of the sinuses, the organ is about normal in consistency; later it becomes firmer and harder, in consequence of increase of the trabeculæ and consecutive atrophy of the lymphoid elements, particularly the Malpighian bodies. Considerable diminution in the size of the spleen may follow gastro-intestinal hemorrhage, severe diarrhœa, etc. Chronic perisplenitis occurs in about one-third of the cases; it may be localized or generalized.

The enlargement of the spleen is usually thought to be due to two factors: (1) Toxemia, bacterial or other toxins brought to the organ by the general circulation—which is especially operative during the early stages, since enlargement is not frequently observed early, before there is any evidence of portal obstruction; and (2) passive congestion—which is especially operative, although not the sole factor, in the later stages; undoubtedly it distends the blood spaces, and, obstructing the return circulation, it serves to retain irritating poisons in the organ.

The *gastro-intestinal tract* shows lesions due in part to the cause of the

cirrhosis (alcoholism especially), in part to portal obstruction. The œsophagus shows general congestion, thickening of the mucosa, and in 80 per cent. of cases, dilated and tortuous veins, especially toward the lower end; these not infrequently rupture and cause severe and even fatal hemorrhage. The *stomach* is the seat of chronic gastritis, often associated with small superficial ulcers or abrasions; pigmentary infiltration, especially toward the pylorus; and dilated veins, especially toward the cardia; these also frequently rupture. The intestines reveal the ordinary lesions of chronic passive congestion and chronic enteritis with pigmentation. The rectum is often congested and the seat of small superficial ulcers and of dilated veins (hemorrhoids), both of which may lead to more or less severe hemorrhage. The *peritoneum* usually shows dilatation of the bloodvessels; often it is inflamed and chronically thickened, participating, on the one hand, in causing the ascites, and on the other hand, leading to thickening and distortion of the omentum and the mesentery with consecutive thickening and shortening of the small intestine (a reduction of eight to ten feet in length may occur). *Tuberculous* infection of the peritoneum is common, occurring in 9 per cent. of the fatal cases (Rolleston), and being more common in cirrhotic males than in other male subjects. It is often responsible for the fatal issue. It is sometimes latent and found only at the necropsy; in other cases it dominates the clinical picture. The *pancreas* is enlarged, swollen, and fibrotic, but there is no constant relationship between the size and the degree of fibrosis of the pancreas and of the liver; the parenchymatous cells show fatty degeneration and pigmentation; the islands of Langerhans are intact, except in the cirrhosis of hemochromatosis, in which they become destroyed.

The *kidneys* show deviations from the normal in about one-half of the cases. In most of these cases they are simply enlarged, or they exhibit the lesions of chronic passive congestion. In some cases, and usually early, albuminuria is encountered; later, distinct fibrosis occurs in 25 per cent. of the cases (110 of 440 cases collected by Rolleston). Few of these cases are due to the cirrhosis *per se;* both are usually due to a common cause (alcoholism), and both, as well as arteriosclerosis, occur at the same period of life and predominantly in the male sex.

The *heart* is often fibroid and fatty (alcoholism, arteriosclerosis), and consequently dilated. Endocarditis may occur as an accidental complication and the pericardium may contain a considerable excess of fluid (partly inflammatory, partly transudation). Arteriosclerosis is common, occurring in more than 60 per cent. of cirrhotic subjects; but it is not due to the cirrhosis (the blood-pressure is low in cirrhosis); both are more likely due to common causes—alcoholism, etc.

The *lungs* exhibit no characteristic lesions; but with the peritoneum they constitute the most frequent seat of tuberculosis in cirrhotic subjects. The tuberculosis may be acute or chronic, latent or obvious; and it leads directly to death in from 12 to 15 per cent. of the cases of cirrhosis (Rolleston). Right-sided pleuritis, due to transport of inflammation through the diaphragm from a perihepatitis, occurs in about 10 per cent.

Pathogenesis.—In portal cirrhosis, in consequence of the activity of some poison, larger or smaller areas of the liver tissue, that is, of the cell mantles about the central veins, become necrotic and are removed—whereby the central veins become more or less uncovered, thus on cross-section appearing eccentrically situated in more or less misshapen lobules; in some cases in which the destruction of liver cells has been through the entire radius of the cell mantle, the central vein may be entirely exposed and may even be found in the interlobular connective tissue, in which event it is very likely to be mistaken for a branch of the portal vein. The cells destroyed are those about the periphery of the lobules—in the area of portal distribution, conforming to the fact that the etiological factor is usually carried by the portal vein. Following the primary destruction of certain liver cells, the intact cells, exhibiting a remarkable regenerative capacity, attempt to replace the lost cells and sometimes succeed in restoring more or less completely the volume of the cell mantles. The cells that regenerate are those in the immediate vicinity of those that have become necrotic, that is, in the ordinary case in which the destruction is not widespread, cells toward or at the periphery of the lobule—which thus are not only most exposed to the deleterious influence of poisons carried by the circulation, but in consequence of being better supplied by arterial blood are also better adapted for repair. Kelly was inclined to believe, in view of Opie's researches, that the primary destructive action may be exerted, at least sometimes, in the so-called midlobular zone—at all events, not immediately at the periphery; that the peripheral cells, being better supplied with arterial blood, survive when others nearer the centre of the lobule succumb, and that these peripheral cells also serve as a focus of regeneration, although, of course, the cells nearer the centre of the lobule also regenerate.

The continuing activity of the etiological factor leads to a continuous or recrudescing death of certain old as well as newly formed liver cells, which in turn is followed by renewed regeneration. This continuous degeneration and regeneration ultimately lead to complete transformation of the architecture of the liver; certain lobules are entirely destroyed, others are partly or completely rearranged, some are markedly hyperplastic although tolerably well arranged, some show dendritic and other irregular proliferation, new islets of liver tissue entirely devoid of central veins appear, and, what is especially important, new circulatory conditions—capillary and venous—arise.

Concurrent with the degeneration of the liver cells, the framework of the lobules collapses and participates in the formation of the fibrosis. This ultimately contracts, and on the one hand causes atrophic changes in the liver cells, and on the other obstruction and obliteration of some of the interlobular and intralobular branches of the portal vein; this latter, although it contributes to, is not the sole cause of, the ascites—other important factors being the new circulatory conditions, especially certain changes in the hepatic arterial supply. Ultimately the potentiality for regeneration possessed by the liver cells lessens, and is finally lost, the general functional capacity of the cells being meanwhile compromised by the contracting connective tissue; the degenerative changes

predominate over the regenerative, and the patient dies, if he has not succumbed earlier to an accidental infection.

Symptoms.—Cirrhosis of the liver may remain for many years entirely latent; indeed, in most cases the lesions in the liver are well advanced before the onset of noteworthy symptoms, and the disease not infrequently constitutes an unexpected finding at the necropsy table. Symptomatically the disease has been divided into the pre-ascitic and the ascitic stage; and the symptoms are described as being (1) obstructive and (2) toxic. As long as the collateral circulation is efficient obstructive symptoms are in abeyance.

In a few cases, during the early stages, phenomena attributed to an ill-defined, so-called, active hyperemia of the liver are encountered; that is, the patient complains of ill-defined or vague gastric symptoms, a sense of weight in the right hypochondrium, perhaps short transitory attacks of slight fever, slight jaundice, and actual pain in the region of the liver, which on examination is found enlarged and tender. Such attacks may last several days, disappear, and recur at intervals.

In most cases the early symptoms are an expression of gastro-intestinal catarrh—due partly to portal congestion, and partly, in many cases at least, to chronic alcoholism with acute exacerbations. The patient complains of coated tongue, irregular appetite, flatulence, epigastric distress, especially after eating, sometimes of nausea and vomiting (often in the morning and usually referable to alcoholism), irregular action of the bowels (alternating attacks of diarrhœa and constipation), or habitual constipation, hemorrhoids, etc. The increasing portal obstruction leads to increasing congestion of the gastro-intestinal tract and the spleen, the congestion being doubtless favored by the absence of valves in the portal tributaries. This congestion reduces the functional capacity of the stomach and intestines, limiting the digestive juices and the intestinal secretions, reducing the absorbing power of the intestines, and often inhibiting peristalsis. Constipation increases and tympanites not infrequently ensues. These phenomena, while not diagnostic, are highly suggestive of the disease, especially with a history of alcoholism.

With the progress of the disease the foregoing evidences of derangement of the gastro-intestinal tract become more marked, and the general health becomes impaired; but the first obtrusive manifestation is not infrequently hematemesis or ascites.

Hematemesis is an initial symptom in some cases, and it is a common event some time in most cases. Usually it occurs early—while the liver is large; when not the initial symptom, it is often the first evidence of serious disease (33 per cent. of the cases); but it may occur late, that is, after the development of ascites and when the liver may have become small. The vomiting of blood may come on without warning, especially when the bleeding occurs from œsophageal varices and the blood does not enter the stomach; in some cases it is preceded by distress or pain and faintness, particularly when it comes from the stomach; severe collapse is uncommon; an immediately fatal result is unusual, but it does occur: in one-third of 60 fatal cases collected by Preble[1] the first

[1] *Am. Jour. Med. Sci.*, 1900, **119**, 263.

hemorrhage was fatal. The hemorrhage, as a rule, is large and consists usually of dark, partially clotted blood. A second or a third hemorrhage may occur at short intervals, and perhaps lead directly to death; or repeated hemorrhages may occur for years, eleven years being the maximum (Preble). The hemorrhage may be derived from: (1) Rupture of varicose veins in the œsophagus. These were present in 80 per cent. of the cases collected by Preble; in more than half of these the point of rupture was obvious to the naked eye, but in only 60 per cent. of the cases with œsophageal varices were there the typical signs and symptoms of cirrhosis. (2) Rupture of varicose veins of the stomach, which usually are situated near the cardiac end; the bleeding is sometimes profuse and may lead to a fatal termination. (3) Gastritis, in which event the hemorrhage is due to oozing from distended capillaries and venules. (4) Abrasion of the gastric mucosa, which may proceed to definite ulceration, and is often associated with gastritis. If the hemorrhage does not soon lead to death, it is an important factor in the development of anemia.

With the hematemesis there is usually blood in the stools; but blood may occur in the stools without the vomiting of blood, especially when the bleeding into the stomach is slow, and also when the source of the blood is the intestine, the rectum or hemorrhoids.

Hemorrhage from or into other parts of the body is very common. The tendency of cirrhotic subjects to bleed is well known, and is attributed to toxemia with disturbed nutrition, the result of functional insufficiency of the liver. Whipple[1] has demonstrated that there is a low fibrinogen content of the blood. This is doubtless the underlying factor in some of the gastro-intestinal hemorrhages and in many of the other hemorrhages. Epistaxis and bleeding from the gums are very common. Sometimes the amount of blood lost is large; it may occasion a well-marked anemia, and has proved fatal. Not infrequently the blood is carried to the fauces or pharynx, and may simulate hemoptysis. The larynx occasionally exhibits varices (usually associated with œsophageal varices) which rupturing may lead to severe hemorrhage or a fatal issue. Bleeding from the lungs is not uncommon. Menorrhagia and metrorrhagia occur particularly in the early stages. Hemorrhages, usually petechial, into or beneath the skin, the mucous membranes and the serous membranes (pleura, pericardium, peritoneum) are not rare, although not so common as in biliary cirrhosis.

Jaundice is not a part of portal cirrhosis, but it occurs some time during the course of from 15 to 20 per cent. of the cases. A faint subicteric hue to the conjunctiva and the skin is not uncommon; it may come and go repeatedly, and last a longer or shorter time; it is usually due to a radicular cholangitis. More marked grades of jaundice attributable to inflammation of the biliary ducts are occasionally observed. In the terminal stages more or less marked jaundice may result from associated catarrh of the biliary ducts, duodenal catarrh, compression or kinking of the ducts, or degenerative changes in the liver cells, and the changes of acute yellow atrophy.

[1] *Arch. Int. Med.*, 1912, **9**, 390.

Toxic symptoms may develop at any time but are much less common early than late, but are occasionally observed early in cases that for some time pursue a latent course. Minor symptoms consist of restlessness, weakness, headache, and itching; the itching may precede or be unassociated with jaundice. More severe toxic symptoms comprise: (1) Apathy, stupor, and coma; (2) an active noisy delirium; and (3) convulsions, paralyses, contractures, one of which may alternate with the others. These are often mistaken for those due to uremia; in fact, they are not infrequently related to renal insufficiency.

Cirrhosis of the liver may be afebrile throughout its course; during the terminal stage the temperature may be subnormal; but attacks of fever (100° to 102.5°) are not uncommon. Sometimes these seem to be part of the disease, especially when it advances rapidly; sometimes they are due to attacks of perihepatitis; sometimes they are due to complications. The more continuous fever, which is common late in the disease, is usually due to tuberculosis—of the peritoneum, lungs, etc.

Physical Signs.—The general aspect is often quite characteristic and may suggest the diagnosis. In the early stages there is pallor and sallowness; the face is peculiarly muddy or subicteroid. Later, the patient becomes thin and emaciated; the musculature is soft and flabby; the general integument is dry, harsh, and wrinkled; the face is drawn, occasionally bloated; the eyes are sunken; the conjunctivæ are muddy or subicteric; the cheeks and temples are hollow; the lips are dry and fissured; the tongue is flabby and coated; the gums are spongy and bleed readily; the breath is foul; the skin of the face and cheeks reveals many distended venules that are prone to bleed; nævi consisting of localized stellate varices and so-called mat nævi ("areas of skin of a reddish or purplish color due to the uniform distention of small venules," Osler) may occur on the face, neck, and back; and small capillary, subcutaneous hemorrhages are prone to develop, especially in regions exposed to traumatism. The abdomen is more or less markedly, sometimes enormously, distended, and is in notable contrast to the emaciated face and extremities. The umbilicus becomes everted and has been known to rupture. The abdominal wall reveals enlarged and varicose veins due to the establishment of a collateral circulation. The very obvious communication sometimes established between the superficial epigastric veins and the long thoracic and the mammary veins is due not to the portal obstruction but to interference with the circulation in the inferior vena cava, the consequence of increased intra-abdominal pressure caused, as a rule, by the ascites. The collateral circulation, although often marked, is rarely ample or efficient; sometimes it is apparently so for a time, at least, since an extensive collateral circulation occasionally relieves more or less permanently a previous ascites.

Examination shows the *liver* to be enlarged in most cases, but the size varies considerably in different cases and in the same case at different times. Foxwell has well said that the liver is "enlarged at all stages of the disease, and that whether enlarged or contracted the clinical symptoms and course are much the same," a statement that has been especially emphasized by Dreschfeld, Rolleston, etc. Usually before the onset of

the ascites, and often during the prevalence of the ascites, the lower border of the liver is palpable one, two, or three fingerbreadths below the margin of the ribs in the right nipple line. The liver is often tender, its edge sharp, and its surface irregular; in some emaciated subjects the hobnail surface can be readily appreciated by the palpating hand, but one must be careful not to confuse therewith irregular areas of fat and fibrous tissue in the abdominal wall. In some cases late in the course the liver is considerably reduced in size, but in many cases in which the liver appears to be small it is of normal or increased size and elevated, being pushed up by ascites or drawn up by a paretic diaphragm (due to perihepatitis, etc.); in other cases emphysema may decrease the extent of liver dulness, or adhesions may prevent the descent of the organ on deep inspiration. In any event, whether small or only elevated, the organ can often but not always be palpated. The left lobe is often disproportionately small and not palpable in the epigastrium—which is quite significant of cirrhosis. Notable variations in the size of the liver occur from time to time, and often rather rapidly; the common change consists of the reduction in size of a large liver, but the reverse is not unknown, although it may be temporary.

The *spleen* is usually palpable but as in the case of the liver, tympanites and ascites often interfere with satisfactory examination. Early the spleen is sometimes not notably increased in consistency; later it is usually firm and often tender. It is often much reduced in size by copious gastro-intestinal hemorrhage, severe diarrhœa, the recurrence of ascites after tapping, etc. An unusual enlargement is sometimes a forerunner of hemorrhage, which may be prevented by prompt free purgation.

Ascites is often the first obtrusive manifestation that leads the patient to seek medical advice. Sometimes it is attributed to a definite exciting cause but, as a rule, the onset is gradual and without definite cause, and the accumulation is slow. Occasionally the fluid accumulates with marked rapidity, in which event it is attributable to thrombosis of the portal vein. Ascites is to be looked upon as a late event, although it is not improbable that congestion and transudation of a small amount of fluid into the peritoneum occur comparatively early, in some cases at least; but this is more or less readily absorbed. It is present in almost if not quite all subjects dying of cirrhosis *per se*, but in scarcely more than 50 per cent. of cirrhotic subjects at the necropsy table. Klopstock found ascites in 172 of 250 cases of cirrhosis that came to necropsy. There is no direct relationship between the size of the liver and the onset or the degree of ascites; in most cases the liver is larger than normal at the time of development of the ascites; but a large liver may be present without ascites; a small liver is rarely found without ascites. It is believed by many observers, such as Hale White, Rolleston, etc., that ascites is really a terminal event, and that if, in a case presumed to be cirrhosis of the liver, the patient lives to require a second tapping, the cirrhosis is complicated with chronic peritonitis (perihepatitis), or the diagnosis is incorrect.

Some patients require repeated tappings. Casati reports one in whom tapping was done 111 times, and Rumpf a case in which it was done 301

times; but these are most unusual. Usually the tapping is of temporary benefit; the fluid soon reaccumulates, slowly, as a rule, occasionally rapidly. In unusual cases more or less permanent benefit seems to result, doubtless in consequence of the formation of adhesions.

The *ascitic fluid* varies in amount—in the average case from 4 to 8 or 10 liters, but it may be as much as 20 liters, with consequent enormous distention. The fluid is usually pale amber in color, clear, somewhat opalescent, and alkaline; it has a specific gravity of 1.008 to 1.015, and it contains 0.5 to 1 per cent. of albumin, and occasionally also traces of urea, urobilin, purin bodies, sugar, etc. Sometimes it is turbid from associated peritonitis, in which event it is of higher specific gravity and contains more albumin; rarely it is chylous, chyliform, or hemorrhagic—the last usually the consequence of traumatism, or petechial hemorrhages in the serosa, etc. The fluid is sterile, unless there has been secondary infection. The cellular constituents are few and consist of lymphocytes and endothelial cells, with a few erythrocytes and leukocytes.

Varying with the amount of fluid there is more or less displacement and compression of the abdominal and thoracic organs. The liver and the diaphragm are pushed upward and cause embarrassment of the respiration and the heart action, and not infrequently compression and consequent congestion and collapse, and perhaps bronchopneumonia, in the bases of lungs, particularly the right.

The ascites is doubtless due to different factors: portal obstruction, peritonitis (or perihepatitis), and toxemia—which are variously operative in different cases. Portal obstruction is an important, but by no means the sole, factor. Ascites seems a natural consequence of the other manifestations of portal obstruction (hematemesis, collateral circulation etc.), and it is the conspicuous result of complete portal obstruction, such as occurs in portal thrombosis. The cause of the increased portal pressure in cirrhosis is not immediately patent, and probably it is not always the same. In some cases thrombosis of at least some of the portal radicles is found—which serves to explain, in part at least, the increased portal pressure, in some but probably few cases. Usually the increased portal pressure is attributed to obstruction of the portal vessels by the newly formed connective tissue, but doubt has been thrown upon this by Kretz and by Herrick,[1] who believes that an important factor is the communication of the arterial pressure to the portal circulation. Lessening of the portal area is probably also of some significance in increasing the portal pressure. Usually the fluid is not inflammatory but sometimes it is, supporting the view that the ascites is sometimes due in part at least to peritonitis (perihepatitis). In part the ascites may be toxic; an unknown toxin acting on the peritoneum; but this is pure hypothesis.

Œdema is common late in the disease, that is, it comes on after the ascites. It is most marked in the feet and legs, but often involves the trunk, especially the dependent portions; rarely anasarca ensues. The œdema of the lower extremities is referable to interference with the

[1] *Jour. Exper. Med.*, 1907, 9, 93.

venous flow in the inferior vena cava. Œdema of the anterior abdominal wall is sometimes related etiologically to increased pressure in the dilated and tortuous regional veins. Occasionally œdema precedes the development of the ascites, in which event it may be due to one of several factors: it may be toxic, in nature analogous to some of the ascites (hypothesis); it is sometimes due to anemia or to chronic renal or heart disease with dilatation; occasionally it may result from thrombosis of the iliac veins or the inferior vena cava; or it may be due to alcoholic neuritis.

The action of the heart is often impeded by the upward pressure exerted by the ascites. The blood-pressure is usually low, the pulse small and frequently rapid, and the breathing labored. The myocardium is often weak, due to fibroid alterations the consequence of alcoholism, malnutrition, and cachexia. A systolic murmur and other evidences of dilatation may develop. A *venous murmur* is sometimes audible in the epigastrium (dilated veins in the falciform ligament), and sometimes over the spleen. Evidences of cardiac failure are sometimes so marked as to obscure the cirrhosis.

The *blood* shows the changes of secondary anemia. There is no leukocytosis unless there is some associated infection. Late in the disease evidences of considerable toxic disorganization of the blood appear and the blood-findings may simulate those of pernicious anemia.

The *urine* is usually diminished in amount, in consequence of deficient absorption of fluid, the large amount of fluid in the peritoneum, pressure exerted on the kidneys, and decreased blood-pressure; the specific gravity and the color are high; sometimes the urine is reddish in color (urobilin, urates); it is highly acid; sometimes it contains albumin (congestion due to failing heart, parenchymatous changes, nephritis); sugar is rarely present; the chlorides are diminished; the urea is reduced; the ammonia is increased (effort to neutralize acid intoxication); indican, albumoses, leucin, tyrosin, and increased volatile fatty acids may be found. Alimentary levulosuria may be detected. In hemochromatosis sugar is present due to fibrotic and other changes in the pancreas.

Complications.—The cirrhotic subject is peculiarly susceptible to infections, both acute and chronic. *Tuberculosis* is the most common (more in adults than in children) and shows a special predilection for the lungs and the peritoneum. It is often overlooked, because unsought; it should always be suspected when there is fever otherwise unaccounted for. In some cases the lung involvement is altogether latent; in other cases it gives rise to physical signs sufficient for diagnosis, but no obtrusive symptoms; in a few cases it dominates the clinical picture. Tuberculous peritonitis is common, and not infrequently determines the fatal issue. It is often overlooked, the ascites naturally being attributed to the cirrhosis; it is suggested by the presence of fever, tenderness and rigidity of the abdominal wall, perhaps increase in the amount of ascites previously stationary (the fluid sometimes becomes hemorrhagic), more rapid course, and more speedy death. The cirrhosis is undoubtedly primary in the great majority of cases, but some believe that in some cases the tuberculosis of the peritoneum is primary and the cirrhosis secondary.

Tuberculous *pleuritis* is not rare, but non-tuberculous pleuritis also

occurs. The pleuritis may be primary or secondary to disease of the lungs or the peritoneum; in the latter case the infection doubtless travels through the diaphragm. The pleuritis is usually right-sided, but it may be left-sided or bilateral. Some care is required in diagnosing right-sided pleuritis, since compression of the lung by a large liver or ascites may occasion dulness and other signs simulating pleural effusion.

Evidences of involvement of the kidneys occur in about half of the cases. In some cases there is only a slight albuminuria, attributable to toxic degeneration of the renal epithelium or passive congestion; in other cases there are signs significant of parenchymatous nephritis; in most cases (almost one-fourth of all cases of cirrhosis) the common manifestations of interstitial nephritis occur.

Peripheral alcoholic *neuritis* occurs in a considerable proportion of cases, and is often overlooked or the symptoms are misinterpreted. A number of acute infections, especially pyococcic infections endocarditis, pneumonia, etc., are not uncommon, and may determine the fatal issue.

Diagnosis.—This is not always an easy matter in the early stages, but it should be made more frequently than it is. In an alcoholic subject with dyspepsia, an enlarged and tender liver suggests the diagnosis; and this is virtually confirmed if to these there be added an enlarged spleen, perhaps recurring attacks of pain in the region of the liver with slight fever or slight jaundice, and urobilinuria. If the diagnosis were made upon these symptoms and the patient treated accordingly, many subjects doubtless would not later exhibit the typical phenomena of advanced cirrhosis; in some perhaps the diagnosis would be incorrect, but in many the disease would be arrested—of the possibility of which the lesions in the hepatic parenchyma afford abundant testimony. Later, when hematemesis, ascites, the hepatic facies, etc., have appeared, the diagnosis can be no longer in doubt.

Little difficulty is likely to be experienced in differentiating *biliary cirrhosis*, which, aside from its rarity, occurs in younger, usually non-alcoholic subjects, and is characterized by persistent jaundice, an enlarged, smooth liver, much enlarged spleen, the absence of all signs of obstruction of the portal circulation, and a very chronic course.

When the liver is enlarged and there is no ascites, one must exclude other causes of enlargement of the liver, such as passive congestion (chronic cardiac or pulmonary disease, cyanosis, usually marked enlargement and tenderness of the liver, some jaundice, urinary signs of congestion of the kidneys, etc.); fatty liver (rather soft and smooth liver, causes of fatty disease of the liver, such as tuberculosis, etc.); amyloid disease (causes of amyloid disease, involvement of other organs, spleen, kidneys, etc.); or leukemia (examination of the blood, etc.). Syphilis is suggested by a history or other evidences of syphilitic infection, more local distress and pain due to the more marked perihepatitis, irregular enlargement of the liver especially of the left lobe, and more common jaundice.

The occurrence of hematemesis and other gastro-intestinal hemorrhages necessitates differentiation from gastric and duodenal *ulcer*. This is often difficult, but cirrhosis is suggested by a history of alcoholism,

enlarged and tender liver, an enlarged spleen, absence of marked evidence of hyperchlorhydria (hyperchlorhydria may occur in cirrhosis), absence of localized epigastric tenderness, etc. In some cases of cirrhosis the hemorrhage is due to associated gastric or intestinal ulceration, which, however, is commonly not of the peptic variety. Hematemesis, especially if small in amount, may also suggest *carcinoma* of the stomach; but in cirrhosis there are no signs of pyloric obstruction or the evidence of carcinoma afforded by the gastric contents and a tumor is not palpable; indeed, in cirrhosis there is more likely a void in the epigastrium rather than a sense of increased resistance. In the event of gastric carcinoma signs of involvement of the liver are likely to supervene sooner or later, so that ultimately the differential diagnosis has to be made between cirrhosis and secondary carcinoma of the liver; alcoholism, long-continued dyspepsia, and enlargement of the spleen are much in favor of cirrhosis. Should the primary growth be elsewhere than in the stomach, there may be localizing signs or symptoms, and perhaps metastases elsewhere, as in supraclavicular or other glands, etc. Splenic anemia, or Banti's disease, may be excluded by the primary enlargement of the spleen, the early anemia, the later development of signs of portal obstruction, and the comparative youth of the subjects—twentieth to the fortieth year.

When ascites has developed one must exclude other causes of ascites, especially chronic peritonitis and perihepatitis (multiple serositis), thrombosis of the portal vein, tumors of the peritoneum and the abdominal organs, chronic cardiac disease, and cachectic states. As already stated, the ascites in many cases of cirrhosis is due, in part at least, to peritonitis or perihepatitis, but in other cases it may be due solely to perihepatitis, occurring alone or as part of multiple serositis, or in tuberculous peritonitis. *Tuberculous peritonitis* is suggested by the absence of a history of alcoholism and of evidences of portal obstruction, and by the presence of fever, tenderness and rigidity of the abdominal muscles; should the tuberculous peritonitis be secondary to cirrhosis with ascites, there may be rather sudden increase in a previously stationary ascites, a more rapid course, and speedy death.

Thrombosis of the *portal vein* occurs in one-third of the cases of cirrhosis, and is suggested by sudden development of ascites (or sudden increase in the ascites, if already present), rapid enlargement of the spleen, severe (perhaps repeated) hematemesis, and rapid recurrence of the ascites after removal; the sudden onset of these symptoms in the absence of a history of alcoholism suggests primary thrombosis of the portal vein, but in many cases of supposed primary thrombosis there has been a latent cirrhosis until this event.

In the ascites of *tumors* of the peritoneum or the abdominal viscera, the seat of the primary growth may be more or less obvious, metastases may be found in the supraclavicular fossa, in glands, about the umbilicus, along the course of the falciform ligament of the liver, etc.; emaciation and cachexia are more marked than in cirrhosis, and signs of portal obstruction are wanting; should the liver or biliary ducts be involved, there is also deep jaundice and nodular and progressive enlargement of the liver. The ascites of chronic cardiac disease is recognized by detect-

ing the disorder of the heart or an antecedent pulmonary disorder with consecutive hypertrophy and dilatation of the heart; the œdema of heart disease begins usually in the legs and other dependent portions of the body (only exceptionally giving rise to primary ascites); and the œdema and ascites, as well as the size of the liver, vary with the functional activity of the heart, responding, therefore, to cardiac tonics.

The ascites of cachectic states, such as advanced nephritis, amyloid disease, leukemia, various anemic conditions, convalescence from typhoid and other infections, is usually slight in grade, often only part of the general anasarca, and is associated with readily recognizable disorders; only when there is associated cardiac or hepatic disease does the ascites become at all marked.

In some cases of ascites the liver is small—in which event the disorder may be syphilis of the liver, advanced passive congestion (red atrophy), chronic deforming peritonitis and perihepatitis, thrombosis of the portal vein, etc. Each of these should be readily differentiated. The small size of the liver may also be due to acute yellow atrophy superadded to cirrhosis of the liver—which also should be readily recognized.

Examination of the fluid aids in diagnosis. The transudate of cachectic states is clear, pale-amber colored, and limpid; it has a specific gravity of 1.010 or less, and contains less than 1 per cent. of albumin; its cellular content is slight and consists of a few lymphocytes and endothelial cells, and perhaps an occasional erythrocyte. The transudate due to mechanical obstruction is clear-amber colored; it has a specific gravity of 1.008 to 1.014, and contains from 1 to 3 per cent. of albumin; its cellular content consists of a few lymphocytes and endothelial cells, a few erythrocytes, and an occasional polynuclear leukocyte. The inflammatory exudates may be serous, serofibrinous, purulent, or hemorrhagic in character; even the serous exudates are usually slightly turbid; they have a specific gravity of 1.015 or more, and they contain from 3 to 6 per cent. or more of albumin; their cellular content consists of lymphocytes, polynuclear leukocytes, endothelial cells, and erythrocytes in varying proportion, depending upon the nature of the infection; lymphocytes in large numbers (upward of 90 per cent.) indicating tuberculous infection, disproportionate polynuclear leukocytosis indicating pyococcic infection. In tuberculous peritonitis and in malignant disease of the peritoneum the fluid is often quite obviously hemorrhagic. The tuberculous nature of the process may be further demonstrated by animal inoculations and tuberculin reactions. That the fluid is due to malignant disease may be proved by finding cells with asymmetrical karyokinetic figures. Occasionally the fluid is chylous or chyliform. The figures relating to the specific gravity and the percentage of albumin are often modified by the occurrence in the one patient of two or more conditions that give rise to ascites.

Special Types.—Certain special types of portal cirrhosis may be differentiated, of which the following are the more important: (1) Cirrhosis of hemochromatosis; (2) malarial cirrhosis; (3) anthracotic cirrhosis; and (4) cirrhosis in children.

Cirrhosis of Hemochromatosis (or Bronzed Diabetes).—This is a rare disease. Futcher,[1] in 1907, was able to find references to only 35

[1] *Am. Jour. Med. Sci.*, 1907, **133**, 78.

undoubted cases, and Potter and Milne[1] in 1912 collected 51 cases. The disorder is most common in men (33 of 35 cases) between the ages of thirty and sixty-one years, but it is most common during the fifth decade. Its characteristics are pigmentation of the viscera and usually also of the skin, cirrhosis of the liver, and fibrosis of the pancreas with involvement of the islands of Langerhans and consequent diabetes. The pigments become deposited in the tissues; the visceral pigmentation antedates that of the skin. The liver, as a rule, is most markedly affected. In the liver and the pancreas, especially, fibrotic changes develop with the pigmentation and degenerative changes in the parenchyma; in advanced cases these reach a high grade, and in the pancreas ultimately involve the islands of Langerhans and lead to diabetes (but death may ensue before this happens). The sequence of events may be described as hemolysis, chronic interstitial hepatitis and pancreatitis, and diabetes. The liver is usually enlarged and presents the common appearances of portal cirrhosis; it is, however, manifestly pigmented, reddish, resembling brick dust or iron rust. The spleen is enlarged, firm, and pigmented.

Etiology.—Mallory[2] believes that chronic copper poisoning is the most potent cause and reports 9 cases observed in one year.

The *symptoms* are those of cirrhosis in its early stage, especially the dyspeptic symptoms, and pain in the right hypochondrium; usually also there is progressive weakness. Occasionally the onset may be sudden. The noteworthy signs consist of general cutaneous pigmentation (suggesting Addison's disease), enlargement of the liver and the spleen (quite like that of ordinary portal cirrhosis), and the ultimate development of diabetes. Ascites may be slight or absent; hemorrhages may or may not occur, but death may result from rupture of œsophageal varices, or there may be purpuric attacks. Diabetes when it supervenes is severe; acidosis is common and usually leads to coma.

The *diagnosis* is apparent from the cutaneous pigmentation, enlargement of the liver and the spleen, and diabetes. The cutaneous pigmentation must be differentiated from that of argyria; of chronic jaundice (in which the scleræ are involved); of Addison's disease (in which there is no enlargement of the liver and spleen and no diabetes); and of ochronosis (alkaptonuria).

The *prognosis* is bad, although life may be prolonged for many years. Death may occur suddenly from rupture of œsophageal varices, etc.; usually it occurs within a year after the appearance of glycosuria.

The *treatment* in the early stages is that of cirrhosis; in the later stages, that of diabetes.

Malarial Cirrhosis.—Many observers doubt that malaria ever causes cirrhosis. It has been suggested that conditions formerly thought to be malarial cirrhosis are the results of kala-azar. Malarial cirrhosis unquestionably is rare in temperate climates; but in view of the marked lesions produced in the liver by malaria, especially severe attacks, there can be no good reason for doubting that malaria may cause cirrhosis.

[1] *Am., Jour. Med. Sci.*, 1912, **143**, 46.
[2] *Am. Jour. Path.*, 1925, **1**, 117.

Anthracotic cirrhosis is a rare disorder of the liver, described by Welch, and associated with the presence of carbon dust (analogous to coal-miner's lung). Adami has described a similar condition.

Cirrhosis in children is by no means rare. Usually it is of the common or portal type; it may be of the biliary type; in congenital syphilis there is a so-called pericellular cirrhosis; and fibrotic lesions sometimes designated cirrhosis are found associated with congenital obliteration of the biliary ducts.

The portal cirrhosis of children is due to the usual causes and is not uncommon in several members of the same family, which may be due to familial habits as regards alcohol, etc., and to the influence of congenital syphilis, which although cured may leave the liver susceptible to the common causes of portal cirrhosis.

The *symptoms* in general conform to those in the adult. Hematemesis is less common (greater distensibility of the spleen in children), diarrhœa and slight jaundice are more common; the liver and the spleen are disproportionately larger than in adults (relative greater volume and more ability for repair in children); tuberculous peritonitis is common and perhaps accounts for most of the ascites and the not uncommon fever.

Prognosis.—On the whole, the outlook in portal cirrhosis is not encouraging. There is much evidence that the liver cells early in the disease and often for a long time undergo considerable hyperplasia in an effort to compensate for the damage, and the collateral circulation is additional evidence of efforts in the same direction; there is reason to believe, therefore, that if early recognized and properly treated the disease could often be brought to a standstill, perhaps cured. As a matter of fact, when recognized early, marked benefit is often obtained. The size of the liver is of comparatively little prognostic significance, although a very small liver is indicative of the later stages; however, the liver may be enlarged from the beginning to the end. Hematemesis does not make the outlook hopeless, since it is sometimes an early symptom and may lead the patient to mend his ways. With the onset of ascites the prognosis becomes distinctly bad, since ascites must be looked upon as a terminal event in the ordinary course of the disease; sometimes, however, the ascites becomes stationary or subsides, in consequence of the establishment of an efficient collateral circulation, and the patient may live for many years. The prognosis is also bad in the event of anasarca, emaciation, cholemia, failure of the heart or the kidneys, and any of the complications and secondary infections. Ordinarily the disease runs a fatal course within three years from the onset of symptoms; but sometimes arrest ensues and the patient may live for a number of years—eight or ten. Occasionally the course is rapid, six or eight months, especially in young subjects much addicted to alcohol; in these cases there are often serious degenerative changes in the hepatic parenchyma, and a form of severe jaundice may ensue and lead to the fatal issue.

Treatment.—This to be effective must be instituted during the formative stage; little beneficial effect can be expected after the destruction of much hepatic parenchyma and the overgrowth of much fibrous tissue. The only trustworthy treatment is based upon our conception of the

etiological factors, and consists essentially in the avoidance of all causes known or suspected to lead to the disease. Of these, the most important are alcohol, stimulating and highly seasoned foods, foods likely to undergo fermentation in the intestinal tract, etc., all of which must be strictly prohibited. In the early stages, alcohol in all forms (including medicinal agents, tinctures, etc.) must be absolutely interdicted; there can be no question that the likelihood of improvement or arrest of the disease depends more upon the non-use of alcohol than upon any or all other factors. But when the disease is well advanced and cure or notable improvement is manifestly impossible, it is not always necessary or wise to discontinue alcohol entirely; the question must be decided for each patient. Although it may be quite obvious that the patient's condition is the consequence of the misuse of alcohol, it does not follow that the disuse of alcohol will result in improvement; he may have become so accustomed to alcohol and so dependent upon it that its withdrawal will be attended by more ill consequences to the general economy than by good results to the liver. In these cases the alcohol should be reduced to the smallest possible amount and this should be given well diluted with the meals. Nux vomica or strychnine is often an excellent substitute for alcohol, and is otherwise beneficial; in some cases, after its use for a time, the alcohol may be entirely withdrawn.

The *diet* of the utmost importance. Milk is the best food; it is nourishing, readily digested and its protein is easier utilized by the liver than that of meat; it leaves little residue, and it is somewhat diuretic. Occasionally, however, it is not well tolerated, especially if the milk is very rich in fats. In almost all cases it should form the only diet, for a time at least—four to six weeks, depending upon the improvement. Two to 3 quarts should be given during the twenty-four hours. Sodium bicarbonate or one of the natural alkaline waters, such as Vichy, etc., may be added to the milk with advantage; or it may be flavored with vanilla, tea, coffee, chocolate, cocoa, etc. If the milk seems to disagree, skimmed milk, buttermilk, or koumyss (less desirable on account of the contained alcohol) may be tried; in exceptional cases it may be necessary to peptonize the milk. At the end of from four to six weeks in ordinary cases, if improvement has occurred, the diet may be increased by the addition of eggs, gruels, cereals, and stewed fruits, and from time to time some fish or green vegetables may be permitted . After a month or more depending upon the condition, the absolute milk diet should be again given for several weeks; thus alternating, the diet should be continued indefinitely. In general, meat, all highly seasoned and stimulating foods, spices, tea and coffee, etc., should be prohibited, because of their irritating effect upon a damaged liver; the use of carbohydrate foods and of fats and eggs also should be carefully supervised, since carbohydrates not uncommonly undergo fermentation, the fats may lead to the formation of fatty acids, and the eggs may increase the formation of cholesterol, all of which may provoke or increase the lesions in the liver. One must individualize, however: in some cases occasional dietetic relaxations are attended by mental as well as bodily satisfaction, a more hopeful outlook, and more or less improvement. In general the consumption of meats, fats, and eggs should be reduced at least 50 per cent.

Comparatively little can be done to influence directly the lesions in the liver, but it is always well to try the effect of iodide, in the hope that it may do good, and with the knowledge that should the lesions be syphilitic benefit will follow. Minute doses of mercuric bichloride (gr. $\frac{1}{30}$ to $\frac{1}{100}$ thrice daily), perhaps combined with iodide, or ammonium chloride, or nitrohydrochloric acid, also seem to do good in some cases. Rolleston warns against the use of arsenic, believing that it may cause cirrhosis. The use of the alkaline waters or ammonium chloride perhaps retards the development of the terminal acidosis. The use of organic preparations of liver has proved of no value whatever.

Special attention must be paid to the gastro-intestinal tract: indigestion, nausea, vomiting, constipation, diarrhœa, etc., must be prevented as far as possible, and when present should be efficiently treated. In the early stages much benefit may follow a course of treatment at some spa, such as Carlsbad, Vichy, etc. The purgative waters have a good influence in lessening the intestinal catarrh and the portal congestion, and in riding the system of toxins; or one may give sodium sulphate or phosphate, magnesium sulphate, etc., as well as an occasional dose of blue mass or calomel. The good effect of free catharsis is often seen in diminution in the size of the liver and spleen.

Improvement has followed the use of biliary tract drainage by the duodenal tube, especially when the continuous method is followed. This is due to (1) the cleansing of the gastric mucosa by the preliminary lavage, (2) the cleansing of the duodenal mucosa and flushing of the intestinal tract by the duodenal lavage (or enemas) and, most important, (3) the flushing of the intra- and extrahepatic bile passages and the removal from the body of toxic substances in the bile of as yet unknown nature, (probably enterogenic) thus favoring regeneration of liver cells by sparing them from the injury of part of the accumulating toxic dose. When added to the orthodox management described above, further improvement has been secured. Its use should be instituted early.

The indigestion, nausea, and vomiting are to be treated on general principles; often the disuse of alcohol is followed by immediate improvement in these symptoms; in other cases the additional use of the purgative waters, or saline aperients, is all that is required to secure the desired relief. In other cases, however, medication is required. In one class of cases, sedatives, such as the different preparations of bismuth, carbolic acid, dilute hydrocyanic acid, and hyoscyamus or belladonna, etc., may be desirable; in another class (subacidity) diluted hydrochloric acid, nux vomica, strychnine, and the bitter infusions may aid. Diarrhœa should not be indiscriminately checked, since it may serve a useful purpose of elimination; but when severe and exhausting, it should be met by regulation of the diet and the use of astringents and perhaps small amounts of opium. Pain and distress in the region of the liver may be relieved by hot fomentations or a cold compress locally, abdominal massage, the administration of ammonium chloride, and depletive measures.

Hematemesis calls for treatment similar to that of bleeding in gastric ulcer. The patient should remain in bed absolutely at rest, and this should be promoted by morphine; an ice-bag may be applied lightly to

the epigastrium (supported, if necessary); all food and drink should be withheld; to relieve the dryness and thirst the mouth and lips should be moistened, or small bits of ice may be given to the patient to suck, but the water should not be swallowed. Usually the hemorrhage ceases of itself. If there is much shock and collapse, stimulants and saline infusions should be used. For several days after the hemorrhage no food should be given by the mouth; glucose solution can be given by the bowel. The after-treatment is analogous to that of gastric ulcer.

The onset of severe nervous symptoms (cholemia, acidosis) calls for treatment required in uremia—free purgation, sweating, and diuresis (hot applications to the loins, large amounts of water, alkaline diuretics, digitalis, etc.), and saline infusions. Should diacetic or other acids be present in the urine, sodium bicarbonate may be given internally and added to the saline infusion. A single, short biliary-tract drainage may tide the patient over the period of immediate danger.

Ascites may sometimes be favorably influenced by the use of purgatives and diuretics. Ammonium chloride 150 gr. (gm. 10) a day, combined with novarsurol, is stated to be of great benefit in relieving ascites and anasarca.[1] In many cases medicinal measures are, however, of little if any value in ascites, especially if the amount of fluid be large; resort, therefore, must be had to tapping. This is indicated when the fluid causes local discomfort, dyspnœa, pulmonary congestion, oliguria, etc. There is no advantage in delaying tapping when it has become indicated; indeed, the resort to tapping as often as it may be indicated may lead to the development of adhesions which may augment the collateral circulation. When done under aseptic precautions, the danger of infection may be disregarded; when the fluid is withdrawn slowly there is little likelihood of collapse. The tapping may be done with a trocar and cannula in the median line midway between the umbilicus and the pubes (after preliminary catheterization of the bladder). Continuous drainage is sometimes practised, but does not commend itself. It has been recommended that the fluid removed by aspiration should be utilized for autoserotherapy, injecting it subcutaneously in small amounts every other day. A small amount of epinephrine has been injected into the abdomen at the completion of a tapping with beneficial results at times.

Operative Methods of Treatment.—Operative relief of the ascites and of the condition upon which it depends, has been undertaken with some success. The procedure, known as the Talma-Morison-Drummond operation[2] (omentopexy, epiplopexy), has for its object relief of an obstructed portal circulation, the diversion of the portal blood to the general systemic circulation through adhesions and consequent increased vascularity between the liver, the omentum, the parietal peritoneum, etc. The immediate mortality ranges between 20 and 35 per cent. How the operation benefits has been much discussed. Rolleston points out that the beneficial results cannot be due solely to diversion of the portal

[1] Rowntree, Keith and Barrier: *Jour. Am. Med. Assn.*, 1925, **85**, 1187.

[2] Consult Drummond and Morison: *Brit. Med. Jour.*, 1896, ii, 728; White: *Brit. Med. Jour.*, 1906, ii, 1287 (227 cases); Morison, *Brit. Med. Jour.*, 1920, i, 1912; Gibbon and Flick, *Ann. Surg.*, 1922, **75**, 449 (literature); Mayo, W. J., *Ann. Surg.*, 1924, **80**, 419.

blood to the general systemic circulation, since this, imitating an Eck fistula, should tend to provoke or increase toxemia. He suggests that the benefit may be due to: (1) Diminution in the flow of blood through the liver, in consequence of which it is enabled to deal more satisfactorily with the blood that does pass through it, and thus reduces the toxemia which is probably an important factor in inducing the ascites; and (2) relief of the venous engorgement and a consequent freer supply of arterial blood consequent upon the vascular adhesions over the surface of the liver, as a result of which the nutrition of the liver cells is improved. Of 227 cases collected by Sinclair White, 84 (37 per cent.) resulted in cure and 29 (13 per cent.) in improvement; 34 (15 per cent.) were failures, and death ensued in 75 (33 per cent.). The operation should be done early, while there is hope that sufficient hepatic tissue still remains to discharge reasonable demands. The patients should be carefully selected; associated cardiac, pulmonary or renal disease, repeated tappings, severe jaundice, toxemia and emaciation are generally considered contra-indications. Rosenstein[1] performed the operation known as "Eck's fistula," an artificially formed anastomosis between the portal vein and the inferior vena cava, for the relief of a case of cirrhosis with marked ascites. He reports that the accumulation of fluid was less rapid than before the operation.

Gibbon and Flick eliminate the surgical step of producing friction of the liver, spleen and diaphragm, thinking that it induces greater post-operative shock.

All writers point out that often operation is too long deferred to secure good results. The high mortality of the earlier Talma operation appeared largely due to the use of abdominal drainage causing peritoneal infections. In such patients, the peritoneum is unusually vulnerable. In the experience of W. J. Mayo, the portal type of cirrhosis responds best to omentopexy alone or combined with splenectomy; the secondary splenic type of portal cirrhosis occurring in late stages of splenic anemia, responds best to splenectomy; the biliary form of cirrhosis is not as favorable for omentopexy or splenectomy but responds best to cholecystectomy and the release of obstructive lesions interfering with proper bile flow.

Biliary Cirrhosis.—Biliary cirrhosis is a chronic disorder of the liver, probably infectious in origin, characterized anatomically by radicular cholangitis and connective-tissue hyperplasia, and clinically by chronic jaundice and enlargement of the liver and spleen. It is commonly spoken of as Hanot's cirrhosis, hypertrophic biliary cirrhosis with chronic jaundice, in contradistinction to Laennec's, or portal, cirrhosis.

Etiology.—Biliary cirrhosis is especially common during adolescence and early adult life; most cases occur between the twentieth and the thirtieth year; it is rare after the fortieth year, but it is quite common in children (juvenile type), especially in India. In adults about 85 per cent. of the cases (22 of Schachmann's 26 cases) occur in males; in children it is equally common in the two sexes. A seeming hereditary influence is not uncommon and is especially in evidence in the disorder as it occurs

[1] *Archiv. f. klin. Chir.*, 1912, **98**, 843.

in India. The disorder may occur in more than one generation of the same family, and the spleen may be enlarged in members of the family who show no evidence of disease of the liver.

The exact nature of the disease is not known. Some, but not all, subjects are alcoholic, but alcohol plays at most a minor role. In the cases so common in children in India it is not in any way an etiological factor. There is some rather inconclusive evidence that the disorder may be the consequence of infection that provokes a radicular cholangitis but no definite etiological agent has been discovered, nor are the pathways of infection known. That the disorder is an infection is suggested by its sometimes developing after infectious diseases, by the common occurrence of attacks of fever and leukocytosis, and the not rare occurrence of general glandular enlargement. Organisms have been isolated during life in several cases, but the evidence is by no means conclusive that they are related etiologically. The postulated infectious agent is believed by some observers to reach the liver by the general circulation, there being a hemic infection or intoxication of a chronic nature, whence the disease is conceived to be a descending cholangitis; by others the infection is believed to be an ascending infection from the duodenum. The concurrent sometimes antecedent, enlargement of the spleen and the occasional occurrence of general adenitis are looked upon as evidence of some infection; the absence or paucity of dyspeptic phenomena and of catarrhal alterations of the duodenum and of the pancreatic duct at necropsy is in favor of the view that the infection does not occur by the common bile duct from the duodenum, but by the general circulation. The evidence favors the view that the disease is a radicular cholangitis, the consequence of a general blood infection. It seems likely that the poison does not reach the liver by the portal circulation, since portal toxemia probably always gives rise to the common or portal cirrhosis; but should the postulated microörganisms of biliary cirrhosis produce a poison in the spleen, this being conveyed to the liver might induce the lesions of portal cirrhosis, which added to those of biliary cirrhosis might account for some of the cases of so-called mixed types.

Pathology.—The liver is enlarged and weighs from 2000 to 4000 gm.; its shape is maintained, its consistency increased ,and its elasticity diminished. The surface is smooth or exhibits very fine granulations; adhesions sometimes occur, but are not very common. The liver is usually dark olive green in color. The cut surface is dark greenish or yellowish green in color, smooth, or very slightly granular in advanced cases; usually the liver lobules are more or less obvious, sometimes apparently enlarged, and always separated by widened trabeculæ of connective tissue. The gall-bladder and biliary ducts, the hepatic artery and veins, and the portal vein show no abnormalities, as a rule; gall-stones are rarely found, not more frequently than in non-hepatic subjects.

Microscopically there is an overgrowth of fibrous connective tissue; but the basic and essential process seems to be the radicular cholangitis—which is disclosed by proliferation and desquamation of the epithelium of the small biliary ducts. These lead to obstruction of the lumina of the small ducts, with consequent dilatation of the biliary canaliculi, which

are found distended with inspissated bile and bile thrombi. Branching columns of cells, so-called pseudobiliary canaliculi, in and about the periphery of the liver lobules, constitute a conspicuous feature. Some of these formations result from proliferation of preëxisting bile ducts; but some undoubtedly are derived from proliferation of the liver cells. The liver cells otherwise exhibit comparatively slight changes. The retrograde alterations so common in portal cirrhosis are rare. Apparently for a long time, much longer than in portal cirrhosis, the liver cells can maintain their structural integrity. Acute necrotic or autolytic changes, however, may occur at any time and determine the fatal issue. The new connective tissue occurs in delicate fibrillar bands that not only course between the lobules but also invade the lobules to a greater or less extent (so-called monolobular, unilobular, or intralobular cirrhosis). In some advanced cases the arrangement of the connective tissue is not so regular, so that it imitates the so-called multilobular or portal cirrhosis. The new connective tissue consists in part of elastic tissue, but proportionately less than in portal cirrhosis.

All the organs of the body are bile-stained. The spleen is enlarged, and commonly weighs from 600 to 1000 to 1500 grams or more; in children it may be as large as or larger than the enlarged liver. It is firmer and denser than normally, and often adherent to the adjacent tissues (perisplenitis). Microscopically it reveals lymphoid and endothelial hyperplasia, and fibrosis with consecutive atrophy of the parenchyma. The pancreas usually shows no noteworthy lesions; occasionally a slight periductal fibrosis has been observed. The gastro-intestinal tract shows no noteworthy lesions, in particular no congestive or catarrhal lesions of the duodenum and the diverticulum of Vater. The lymphatic glands in the portal fissure and usually the adjacent glands are enlarged, œdematous, and congested, but they exert no pressure on the biliary ducts.

Symptoms.—The onset is insidious. For a long time there may be ill-defined complaint of poor health, general malaise, weakness, loss of flesh, etc.; or there may be a sense of weight or distress, perhaps actual pain, in the right hypochondrium; rarely there is some dyspepsia, coated tongue, poor appetite, perhaps nausea, diarrhœa, etc.; in a few cases attention is first directed to increase in the size of the abdomen.

In the great majority of cases the obtrusive symptom is jaundice, which is slight at first. The jaundice varies in degree from time to time, but on the whole it tends to increase and eventually it may become extreme, usually greenish; sometimes the markedly bronzed color suggests that of Addison's disease. The usual concomitants of protracted jaundice are seen. There is often intense itching, sometimes xanthelasma, etc. Bleeding from the mucous membranes may occur from time to time for a long period, or there may be recurring attacks of purpura; the urine shows bile pigment. The feces also contain bile pigments and may be very dark.

In addition, the disease is characterized by periodic attacks of more or less severe abdominal pain, especially in the region of the liver, sometimes attended by nausea and vomiting, and associated with fever, leukocytosis, and increase of the jaundice. These attacks occur without

regularity and without demonstrable cause, and they last variable periods—several days to several weeks. Usually the fever does not go above 102°; in some cases there is slight fever for long periods. Occasionally these exacerbations are attended by the phenomena of icterus gravis, and with fever, delirium, coma, etc., the patient may die.

The other manifestations are not characteristic. There may be dyspnœa from impeded action of the diaphragm and pressure upon the lungs and the heart by the enlarged liver and spleen. The myocardium may become disorganized, so that dilatation ensues; the pulse is rarely slowed. Diarrhœa is the rule rather than the exception.

Examination usually reveals an obvious bulging of the lower right costal arch and the upper part of the abdomen, which is found to be due to a much and uniformly enlarged liver; it may reach, in the right nipple line, from the fourth rib, or higher, to near or below the transverse umbilical line; it occupies a proportionate area in the epigastrium; and it extends well into the left hypochondrium. It presents a smooth surface; rarely it may be slightly irregular from fine granulations on the surface (which, however, are scarcely appreciable by palpation) or from adhesions. The organ is firmer than normal, and its edge is sharp and well defined. Usually the enlargement is progressive, although the size of the organ may vary somewhat from time to time. Rarely toward the end some decrease in size may become apparent (usually more apparent than real), attributed to contraction of the newly formed connective tissue or secondary portal cirrhosis. The liver may be moderately but often is not at all tender. The gall-bladder is not enlarged, except in the event of some complication.

The *spleen* is markedly enlarged, much more so than in portal cirrhosis; it is hard and presents a sharp and well-defined edge. Some writers believe that the enlargement of the spleen may antedate that of the liver. In children the spleen may be actually larger and heavier than the enlarged liver—the juvenile type of biliary cirrhosis (*cirrhose biliaire splénomégalique* of Gilbert and Fournier). On auscultation one may sometimes hear a soft murmur or friction (perisplenitis).

The blood reveals oligocythemia, leukocytosis during the periodic exacerbations, diminished coagulability, etc. The urine, usually increased in amount in addition to containing bile pigments, is highly colored and of increased specific gravity; albumin and sugar are usually absent.

Rarely a bulbous enlargement of the fingers (Hippocratic fingers) and toes occurs; it is due to thickening of soft tissues and although it resembles hypertrophic pulmonary osteo-arthropathy, it cannot be correlated with any disease of the lungs; presumably it is due to some unknown toxin, which is not peculiar to biliary cirrhosis, since it may be found in other types of protracted jaundice. In children growth is stunted and the onset of puberty is delayed.

Types of Biliary Cirrhosis.—The varying relations between the size of the liver and of the spleen and the time of the onset of these enlargements have led certain French authors, especially Gilbert, Chauffard, Fournier, to postulate different types of the hypertrophic biliary cirrhosis, depending on the priority of involvement of the liver or spleen and also

on relative amount of enlargement of these two organs. The differentiations are of minor clinical significance, although they suggest that all cases of biliary cirrhosis are not of the same nature and genesis.

Diagnosis.—This, as a rule, presents no unusual difficulties, although it is made more frequently than the rarity of the disease warrants. The important diagnostic features consist of the occurrence in a young, usually non-alcoholic, subject of chronic progressive jaundice, with considerable and persistent enlargement of the liver and spleen, and periodic attacks of abdominal pain, fever, and leukocytosis, with subsequent increase in the jaundice, and no signs of cholelithiasis or portal obstruction.

There should be no difficulty in differentiating the more common or *portal cirrhosis*, which occurs, as a rule, in older and alcoholic subjects and is attended by more marked dyspeptic symptoms and by evidences of portal obstruction. In portal cirrhosis hemorrhages, especially hematemesis, often occur early and are commonly profuse; whereas in biliary cirrhosis hemorrhages are usually a late manifestation and small; they are most common from the oral and nasal mucous membrane and into the skin, and hematemesis is rare. Jaundice sometimes occurs in portal cirrhosis, but it is a complication and catarrhal in nature; in biliary cirrhosis it is the conspicuous feature, and, although permanent, it is not associated with absence of bile from the feces. Constipation is common in portal cirrhosis, diarrhœa in biliary cirrhosis. Portal cirrhosis usually runs a fatal course within three years or less; biliary cirrhosis not uncommonly lasts from five to ten years or more.

The clinical phenomena of biliary and of portal cirrhosis are sometimes combined; that is, jaundice supervenes in a case of portal cirrhosis with enlarged liver and ascites, or ascites develops in a case of supposed biliary cirrhosis with enlarged liver and jaundice. This has led some authors to believe that biliary cirrhosis is not a disease entity; others postulate mixed forms, or the superaddition of portal cirrhosis to the final stages of biliary cirrhosis. The diagnostic difficulties are much simplified by bearing in mind that biliary cirrhosis is a rare disease; that, although jaundice is not an essential part of portal cirrhosis, it occurs in from 15 to 20 per cent. of the cases, being due to a complicating radicular cholangitis; and that inasmuch as the liver is usually enlarged in portal cirrhosis (although it may become small), an enlarged liver with ascites and jaundice does not necessarily mean a mixed form of cirrhosis, but is quite consistent with the natural history of portal or the common type of cirrhosis. On the other hand, the very rare cases in which ascites supervenes after the long continuance of biliary cirrhosis may be variously interpreted: in some cases the ascites may be due to disease of the peritoneum (perihepatitis, peritonitis, etc.); in other cases it may be due to gross obstruction of the portal vein, or if terminal to cachectic states; in other cases perhaps the lesions of portal cirrhosis are added to those of the primary biliary cirrhosis.

When the jaundice is slight and perhaps readily overlooked, other forms of enlargement of the liver, such as passive congestion, fatty liver, amyloid liver, leukemia, tuberculosis, syphilis, and hemochroma-

tosis must be differentiated. Other causes of chronic jaundice also must be excluded, such as cholelithiasis and carcinoma.

Prognosis.—The outlook as to cure is hopeless. The disease usually runs a protracted course, averaging four or five years, but not uncommonly continuing for ten years or more. The periods of remission are often of long duration and the general health may be well maintained; but the exacerbations may be severe and seriously undermine the general resistance, and they may lead to a severe form of jaundice and death. The prognosis is especially bad in the event of severe jaundice with nervous symptoms (fever, delirium, coma, etc.), recurrent hemorrhages, marked general weakness, intercurrent complications, etc.

Treatment.—The treatment is largely symptomatic, and in general does not differ materially from that advised in portal cirrhosis. The hygienic conditions should be the best obtainable, and should comprise much fresh air, non-exposure to cold and damp, moderate and carefully regulated exercise, etc. The diet may be more generous than in portal cirrhosis, but with a view not to provoke gastro-intestinal derangements; the patient should avoid dietetic indiscretions, alcohol, etc. Constipation should be overcome by the use of calomel, blue mass, and the salines.

The probable infectious nature of the disorder suggests the use of antiseptics, such as hexamethylenamine and the salicylates, which are eliminated with the bile. Their use has been followed by some apparent improvement. Good results also are reported to have followed drainage of the gall-bladder and biliary ducts; but the diagnosis in some of the cases is open to question: undoubtedly they may have been cases of infection of the biliary tract, but probably not of biliary cirrhosis. Non-surgical drainage of the biliary tract might be tried as it can do no harm and might prove of value if given early, in short courses of continuous drainage (a week or two at a time).

Wilson's Disease.[1]—Progressive lenticular degeneration, hepato-lenticular degeneration, or what is commonly termed "Wilson's disease," was brought prominently to attention by S. A. Kinnier Wilson who described a fatal malady occurring only in youth or young adults. Although perhaps of greater interest in neurology it is mentioned here because of the constant association of an advanced, though symptomless, cirrhosis of the liver, usually multilobar and atrophic. Wilson defined the condition as follows: "Progressive lenticular degeneration is a disease which occurs apparently only in young people, which is often familial, but not congenital or hereditary; it is essentially and chiefly a disease of the extra-pyramidal motor system, and is characterized by involuntary movements, usually of the nature of tremor, dysarthria or anarthria, dysphagia, muscular weakness, spasticity or hypertonicity, and contractures, with progressive emaciation; with these may be associated emotionalism and certain symptoms of a mental nature. It is progressive and, after a longer or shorter period, fatal. Pathologically, it is characterized predominantly by bilateral degeneration of the lenticular nucleus, and in addition cirrhosis of the liver is constantly found, the latter morbid condition not giving rise to symptoms during the lifetime of the patient."

[1] Consult Wilson, S. A. K.: *Lancet*, 1912, i, 1115; *Brain*, 1911-1912, **34**, 295; *Oxford Med.*, 1921, **6**, 261; Hall, H. C., *La degeneiescence hépato-lenticulaire*, Paris, 1921.

In 1912, Wilson placed on record 6 carefully studied cases of his own, additional to 6 reported in 1890 by Gowers, by Ormerod, and by Homén, under different diagnostic names. Of the 12 cases the youngest was ten and the oldest twenty-six years of age. There were 7 males and 5 females Eight cases were familial. Syphilis and alcohol can be excluded as factors producing the cirrhosis. In these 12 cases, the disease was fatal in four to six months in the acute cases, and three to five years in the chronic cases. In the former, there is an irregular fever, more rapid emaciation and an appearance suggesting a toxic infection. Otherwise, the acute and chronic cases differ in nowise except in duration. Compared with the motor, the sensory symptoms are not striking. Occasionally there is pain in the extremities or body. Wilson states there are no sensory changes in pure lenticular disease. The tendon reflexes are active but not exaggerated; the cutaneous and abdominal reflexes are normal. Mental symptoms are not conspicuous. There may be inconspicuous corneal pigmentation (a greenish haze) in some cases. Eleven of the 12 orginal cases gave no evidence of liver disease during life although cirrhosis was advanced in all; in 2 cases there was a history of jaundice antedating by some years the symptoms of lenticular disease. Among other negative symptoms, Wilson mentions normal optic disks, and pupillary reflexes; no nystagmus; no cerebellar symptoms; and no impairment of sensibility.

Wilson's description of the cirrhosis is as follows: "The cirrhosis of the liver is always advanced and is strikingly apparent. The organ is usually rather smaller than normal, but not constantly so. It is firm, hard, tends to preserve its shape and presents the appearance of rounded nodules of liver tissue clustered together, of the size of hazel nuts or smaller, separated by depressed cirrhotic bands. The organ is never bile-stained but often rather lighter in color than normal. Microscopically, normal areas, necrosed areas, fatty degenerated areas, and actively regenerating areas are found to be scattered irregularly through the organ. The type of cirrhosis is mixed, *i. e.*, it is mostly multilobular, in some places monolobular and occasionally there are indications of intralobular cirrhosis. So-called hypertrophying bile ducts are often seen in the connective tissue formation, which in some places is cellular, in others fibrous." Wilson suggests that: (1) it seems clear that the disease is not due to a congenital or abiotrophic defect; the presumption is strong that the disease is acquired; (2) there is evidence to show that the disease is toxic in origin, but none to suggest that this toxin is syphilitic; (3) it is possible this toxin may be elaborated in the liver; (4) the toxin has a specific action on the lenticular nucleus; and (5) the nature of the toxin is speculative. It is almost certainly not microbial.

Greenfield, Poynton and Walshe[1] found 70 cases reported, 30 of which came to autopsy and in each instance, cirrhosis of the liver was found. A familial element was noted in about one-half of the cases reported, but of those autopsied in less than one-half. Nothing further is accurately known of the pathogenesis of this disease, which is unique in representing advanced, but symptomless, disease in the liver associated with an advanced and symptomatically active lesion in the lenticular nucleus.

[1] *Quart. Jour. Med.*, 1923–1924, **17**, 385 (literature).

CARCINOMA OF THE LIVER

Etiology.—Carcinoma of the liver may be primary or secondary. Primary carcinoma of the liver is a rare disease. Among 11,500 necropsies Hale White[1] found only 11 cases. Secondary carcinoma is more common, the ratio of the primary to the secondary being 1 to 25 (Hale White) or 1 to 40 (Hansemann[2]). Among 4200 necropsies, Hale White found 136 examples of secondary deposits in the liver, of which at least 126 were carcinomatous.

Pathology.—Primary carcinoma of the liver appears under three forms: (1) Nodular or multiple carcinoma. This is the most common form, occurring in 65 per cent. (Eggel[3]). (2) Massive carcinoma is the type occurring in 23 per cent. (Eggel). It appears as a whitish or grayish-white opaque mass, often occupying almost if not quite an entire lobe (usually the right). It is sharply defined from the surrounding hepatic tissue, which is compressed and atrophic, and sometimes contains smaller secondary nodules. (3) Infiltrating or diffuse carcinoma is the type occurring in 12 per cent. (Eggel). One or both of the major lobes of the organ become pervaded by new-growth, and often the seat of considerable new fibrous-tissue formation, so that the macroscopic appearances are similar to and are commonly mistaken for portal cirrhosis (the cirrhosis with multiple adenoma, or with carcinoma, of Hanot and Gilbert, and other French authors). Microscopically the cells in carcinoma of the liver are usually polyhedral in type, and are believed to be derived from the hepatic cells; rarely they are columnar in type, and are then referred to proliferation of the epithelium of bile ducts. Transitional types also occur, which suggests the histogenetic equivalence of the liver cells and the cells of the biliary ducts. In some cases the sequence of events is represented by hyperplasia, adenoma, carcinoma. It is doubtful, however, whether the designation carcinoma with cirrhosis is as widely applicable as maintained by French authors—who believe that this represents one-third of the cases of primary carcinoma of the liver. In perhaps the majority of the cases the condition is merely cirrhosis with considerable hyperplasia of the liver cells (nodular cirrhosis); appearances suggesting carcinoma are sometimes due to softening of some of the so-called "hobnails," with rupture into the hepatic or the portal veins, and to thrombosis—either of which may be the antecedent condition.

Secondary carcinoma appears usually as multiple, whitish, grayish-white, or yellowish-white nodules scattered through the organ, most commonly at the periphery, where they often occasion perihepatitis. Often they become umbilicated and softened or hemorrhagic.

Symptoms.—These are not notably different whether the growth be primary or secondary, although variations occur and, in perhaps one-half of the cases of secondary carcinoma, symptoms referable to the primary growth are not apparent. Usually the onset is insidious; the patient may complain of general ill health, languor, anemia, emaciation, etc.,

[1] *Allbutt's System of Medicine*, 1900, **4**, 204.
[2] *Berl. klin. Wchnschr.*, 1890, **27**, 353.
[3] *Beitr. z. path. Anat. u. Physiol.*, Jena, 1901, **30**, 506 (literature).

for a long time before the true nature of the disorder is disclosed; in many cases, certainly in at least one-third of the cases of secondary carcinoma, the actual conditions are recognized only at autopsy. In some cases symptoms referable to the primary growth precede, for a variable time, symptoms significant of involvement of the liver; but in a considerable number of cases carcinoma of the stomach, rectum, etc., may be for a long time latent; or the symptoms are not obtrusive, and the first noteworthy manifestations may be referable to the liver. In a small percentage of cases the primary growth remains insignificant; the lesions are most marked in the liver, and the symptoms almost if not exclusively hepatic, consisting of local pain and distress, jaundice, ascites, and enlargement of the liver.

Local discomfort is quite common, but even with large carcinoma there may be no actual pain. The sense of discomfort and weight is usually proportionate to the size and rapidity of growth of the carcinoma; it is often increased by the left lateral posture, which increases the tension on the ligaments. Actual pain sometimes occurs, and may be quite severe, in which event it is attributable to a concomitant perihepatitis; it often radiates to the right shoulder, and may be increased by motion. Sometimes there is more or less local tenderness, especially on deep palpation and occasionally there is severe colicky pain.

Jaundice is present in more than half of the cases; it is variable in degree, at first, at least, depending upon its cause, but it tends to increase and become permanent. It may be due to a variety of causes that are often difficult to differentiate. Thus, it is not infrequently due to compression of the common bile duct by a primary growth in the head of the pancreas, or to secondary nodules in the lymphatic glands; it may be due to primary carcinoma of the biliary ducts; or it may be due to pressure on the intrahepatic ducts by sufficiently large nodules, to extension along the lumen of the biliary ducts, or to more widespread obstruction, such as may occur in massive carcinoma. In the last-mentioned instance, if jaundice occurs, which is unusual, it is slight in grade and not associated with clay-colored stools. In the other cases the jaundice is obstructive in origin; it increases in intensity until it becomes of the most severe grade; it is permanent, although for a time, at least, it may vary in intensity; and the stools are clay-colored.

Ascites is somewhat less common than jaundice; it occurs in almost if not quite half of the cases; both occur together in about 20 per cent., in which event the ascitic fluid is bile-stained; otherwise the fluid is pale, of low specific gravity, and contains a small amount of albumin; occasionally it is hemorrhagic or chyliform. It varies considerably in amount, but is usually moderate and often for a considerable time stationary; it rarely requires tapping. Perhaps in some cases the ascites is due to portal obstruction, but this is unusual, since other evidences of portal obstruction are usually absent or in abeyance. In most cases the ascites is due to perihepatitis or peritonitis; in some cases to carcinomatous involvement of the peritoneum.

Progressive enlargement of the liver is the phenomenon that determines the diagnosis. The enlargement may be moderate or very great. Usually

it involves the right lobe more than the left. The liver may increase notably in size under observation. The edge is usually firm and hard, and it, as well as the palpable surface, is quite irregular—nodular. The nodules vary considerably in size; usually they are firm, especially when small, but as they grow they often soften in the centre and hence become depressed or umbilicated; sometimes this umbilication can be made out by palpation, which is quite diagnostic of carcinoma; in other cases they may seem semifluctuating. Sometimes they suddenly increase in size from hemorrhage; occasionally as they degenerate they become smaller. In the massive carcinoma this nodular formation does not occur, but one can often make out marked distortion due to a very large new growth. The gall-bladder can sometimes be palpated at the lower edge of the liver. In a few cases secondary nodules develop along the falciform ligament, and become palpable at or through the linea alba, at the umbilicus; these are conclusive evidence of the real nature of the disorder, but in some cases a microscopic examination of an excised nodule may be required to eliminate tuberculosis.

In many cases the base of the right lung becomes compressed or in other cases the growth in the liver forms an attachment to and finally penetrates the diaphragm, and sets up pleuritis that may become purulent. In rare cases a nodule in the liver penetrates a branch of the hepatic vein, and the carcinomatous cells, being carried to the lung, set up widespread metastasis. Any of these conditions may be responsible for a harsh, dry cough, but in some cases no abnormalities can be detected to account for the cough, which must be attributed to irritation of the diaphragm (perihepatitis) or the pleura, etc. The liver sometimes by reason of its weight or by causing kinking, impedes the circulation in the inferior vena cava, and gives rise to dilatation of the superficial veins of the abdomen (but leaves the region of the umbilicus free—which is a point of distinction from the dilatation due to portal obstruction); in other cases œdema of the feet and legs results from this cause, but, especially in advanced cases, this may be due also to anemia, cardiac weakness, venous thrombosis, etc. Albuminuria is occasionally observed late in the course and is attributable to anemia and toxic degeneration of the renal epithelium (hepatogenous albuminuria, Tessier); indicanuria and increase of the nitrogenous extractives also may be observed. Hydronephrosis may ensue from pressure on the ureter or renal pelvis. Gastrointestinal symptoms are often present, apart from the cases of primary carcinoma of the stomach; vomiting may result from pyloric obstruction (pressure or kinking). The spleen may become enlarged, especially in the event of pylethrombosis or carcinoma with cirrhosis.

In the course of time the patient loses strength and emaciates (rarely, when the liver increases rapidly in size and attains huge dimensions, the weight may remain stationary or actually increase); he becomes anemic and cachectic, and phenomena attributed to cholemia develop.

Diagnosis.—This is not always possible, especially in the cases of secondary growth in which the deposits are few in number, small in size, and deep within the substance of the liver. In cases in which a primary growth is obvious and in which there is a persisting severe jaundice,

cachexia, and a rapidly enlarging and nodular liver, the diagnosis can often be made on inspection alone, especially if the patient be made to take a deep inspiration (whereupon the irregular nodular liver will be seen to descend). Between these extremes lie the majority of cases, in which the diagnosis is often difficult. Should the liver seem to be the seat of disease, one must determine (1) whether a new growth is present; (2) whether, if present, it involves the liver, and (3) if so, whether it is primary in the liver.

Difficulty is sometimes experienced in determining whether a new growth is present, since it may be imitated by fecal accumulation in the colon, and by inflammatory thickenings about the gall-bladder and the biliary ducts. Feces, however, may be indented and pushed about; they change their position from time to time, and they may be removed by cathartics and enemas. In inflammatory thickenings about the gall-bladder there is usually a history of past cholecystitis or cholelithiasis; the mass is in the region of the gall-bladder and is single (that is, there are no other nodules on the surface of the liver); the liver may not be enlarged at all, and if so, the enlargement is slight or moderate and uniform; jaundice, if present, varies from time to time, and may clear altogether (which is practically unknown in carcinoma); and the patient's general health is not so seriously involved.

One must avoid the error of mistaking tumors of adjacent organs for a new growth of the liver. This can usually be done by attention to the symptomatology, a careful physical examination, and by a study of the gastric contents, urine, etc. Tumors of other organs, which are near the liver, may have respiratory movement, but such movement is less common in renal and other retroperitoneal growths, which in addition fill out the loin, are covered in front by the intestine, and do not project so high toward the thorax as hepatic tumors. Tumors of the stomach have a significant symptomatology, often cause dilatation of the stomach, characteristically change the gastric contents, and can usually be found quite separate from the liver. New growths of the omentum, or the thickened indurated omentum of tuberculous or other chronic process, usually have a peculiar elongated or irregular shape and are separated from the liver by a zone of tympany, and the free edge of the liver can usually be felt free and uninvolved.

Should the disorder be definitely located in the liver, one has to eliminate other causes of enlargement, especially cirrhosis, syphilis, abscess, hydatid disease, obstruction of the common duct, passive congestion, constricted liver, leukemia, amyloid disease, fatty liver, etc.

In *portal cirrhosis* there is a history of alcoholism; evidences of portal obstruction are common; the liver usually is uniformly enlarged, although as the disease advances it may grow smaller (in new-growths it continues to increase); the palpable nodules are small, not umbilicated, and not surrounded by intervening areas of smooth liver. *Biliary cirrhosis* occurs, as a rule, earlier in life than carcinoma; the jaundice is early, moderate in grade, and yellowish; since some bile always reaches the intestine, the stools are bile-stained; the liver is uniformly enlarged and smooth; the spleen is enlarged; and the course is less rapid.

In *syphilis* of the liver the pain is often more marked; the liver does not increase so rapidly in size and lessens under the influence of anti-syphilitic treatment; and there is a history or there are signs of syphilis elsewhere. *Abscess* which is sometimes simulated by those cases in which the carcinomatous nodules soften and become semifluctuating, and in which the fever of cachexia, anemia, or terminal infection ensues may be differentiated by the antecedent disorder, by the absence of cachexia, by the less common occurrence of jaundice and ascites, and by the more common fever, etc.

Hydatid disease is much rarer than carcinoma; it develops, as a rule, earlier in life, and is of slower course. The enlargement of the liver is usually single (perhaps double, rarely multiple), smooth, and not tender; the spleen is enlarged; there is seldom jaundice and rarely if ever ascites; and cachexia does not ensue until the disease has lasted a long time.

Having determined the liver to be the seat of carcinoma, it is often difficult, sometimes impossible, to say whether the new growth is primary or secondary. In at least one-third of the cases (in 50 per cent. according to Leube) the primary growth is latent; but in some cases in which it is apparently latent it may be detected upon careful study. Attempts to find it should always be made, since secondary growths of the liver are from 25 to 40 times as common as primary growths. The presence of a growth in the liver is presumptive evidence of its secondary nature; this is rendered more likely by the presence of many nodules (which, however, do not exclude a primary liver growth with secondary nodules); by more marked emaciation; and by the less rapid course and less rapid enlargement of the liver. Primary growths usually are single and cause uniform enlargement of a part of the liver; they less frequently cause jaundice and ascites; and they grow more rapidly and hence lead to less emaciation, but to earlier death.

Prognosis.—The diagnosis, of course, brings with it the prognosis: the outlook is hopeless. Hale White gives the duration of life as four months from the development of symptoms in primary carcinoma, and seven months after the development of symptoms referable to the liver in secondary carcinoma.

Treatment.—This is purely palliative, and has for its object promotion of the comfort of the patient. In rare cases a single growth has been removed by operation. If the patient becomes rapidly worse and the diagnosis of carcinoma remains in doubt, exploration is not only justifiable but should be urged in the hope that carcinoma can be ruled out, and some benefit to the patient be accomplished surgically.

SARCOMA OF THE LIVER

Sarcoma of the liver may be primary or secondary, but it is very rare.[1] Primary sarcoma may occur as a nodular or a diffuse growth, and may originate from any of the connective tissues of the liver or from the

[1] Consult Marz: *Centralbl. f. allg. Path. u. path. Anat.*, Jena, 1904, **15**, 433 (literature).

endothelium of the bloodvessels or the lymphatics (angiosarcoma, endothelioma, perithelioma). Secondary sarcoma may follow a primary growth anywhere else in the body, but it is especially common after sarcomas of the bones, adrenal, mediastinum, and uveal tract; the last mentioned are likely to be pigmented. Several years may elapse after enucleation of an eye on account of melanotic sarcoma before recurrence in the liver occurs. Clinically sarcoma cannot be distinguished from carcinoma, except perhaps in the cases that occur in infants,[1] in whom a tumor is more likely to be sarcomatous than carcinomatous. Sarcoma of the liver runs a rapid course, and soon terminates fatally.

BENIGN TUMORS OF THE LIVER

Benign tumors, such as adenoma, angioma, so-called fibroma, lipoma, etc., are occasionally observed, but are chiefly of pathological interest. Adenomas[2] may be single or multiple, and may develop from the hepatic cells or from the biliary ducts. The biliary-duct adenoma may become the seat of cystic dilatation (cystadenoma or adenocystoma). Another tumor, often described as an adenoma, arises not from liver tissue but from aberrant adrenal in the liver. Multiple adenoma occur chiefly in association with cirrhosis (so-called nodular cirrhosis); the adenomatous formations are really localized compensatory hyperplasias of the liver cells. It is difficult, it not impossible, to distinguish between hyperplasia and adenoma: there is no sharp line of demarcation, and both may progress to carcinoma. The single adenoma cannot be diagnosed unless it becomes very large, when it presents more or less outspokenly the symptoms of carcinoma of the liver. The symptoms of multiple adenoma are those of of the basic condition—cirrhosis.

Angioma is a rare tumor, although it is quite as common in the liver as anywhere in the body. They may be congenital or develop in advanced life; they may be single or multiple, and small or very large. They cannot be recognized clinically. Most of the so-called fibromas and lipomas are not true tumors, and one may well doubt whether such tumors occur in the liver.

CYSTS OF THE LIVER

Cysts may be parasitic or non-parasitic. The parasitic cysts are due to infection with *Echinococcus granulosus*. Non-parasitic cysts may occur alone or in association with cystic disease of the kidneys or congenital anomalies elsewhere. There may be one or many cysts. According to Moschcowitz the cysts, as a rule, are multiple and most abundant in the zone of the liver just beneath the capsule. They vary in size from those that are microscopic to those that occupy nearly the entire liver. They are equally common in the two sexes, and occur at all ages. They are believed to originate in aberrant bile ducts, in consequence of inflammatory hyperplasia or of retention of fluid the result of congenital

[1] Consult Pepper: *Am. Jour. Med. Sci.*, 1901, **121**, 287.
[2] Watzold: *Beitr. z. path. Anat., u. Physiol.*, Jena, 1906, **39**, 456 (literature).

obstruction. The diagnosis may be hazarded from the association of an enlarged liver with tumors in the loins (cystic kidneys) or symptoms of chronic interstitial nephritis.

THE GALL-BLADDER AND BILIARY DUCTS

ANOMALIES OF FORM AND POSITION

Rarely the gall-bladder may be absent, misplaced, or misshapen. When the gall-bladder is absent, the common bile duct not infrequently presents a circumscribed dilatation (analogue to the gall-bladder); a similar dilatation occasionally develops after operative removal of the gall-bladder. Rarely there is a double gall-bladder with two cystic ducts. Furthermore, the gall-bladder may be misplaced—to the left of the transverse fissure; or it may be embedded more or less deeply in the substance of the liver, and more or less completely surrounded by liver tissue; or the fundus may penetrate the liver substance and present on the anterosuperior surface of the liver. Sometimes it exhibits an hour-glass constriction, aside from the consequences of inflammatory changes. The biliary ducts vary in length. There may be little if any common hepatic duct, due to the unusual length of the right and the left hepatic ducts. The cystic duct may not join the common hepatic duct until close to the insertion into the duodenum. The common bile duct and the pancreatic duct may enter the duodenum separately; sometimes the common bile duct enters with the duct of Santorini. Finally the biliary ducts may be congenitally obliterated.

Congenital Obliteration of the Biliary Ducts.—This is characterized anatomically by obliteration or atresia of the biliary ducts and biliary cirrhosis of the liver, and clinically by persistent jaundice and so-called cholemia which proceed to a fatal issue. The disorder was first prominently brought to attention by John Thomson,[1] who in 1892 collected 50 cases; in 1908 Lavenson[2] collected 62 cases. Since then it has been more frequently recognized. Holmes[3] in 1916 collected 108 authentic cases and added 1 of his own. Gordon[4] in 1922 reported 4 cases found among 1086 autopsies. The nature of the disorder has not definitely been determined, at least for all cases. It is likely, as stated by Rolleston[5] that several different conditions may give rise to obstruction or obliteration of the large bile ducts in the new-born, such as peritoneal adhesions set up by fetal peritonitis, syphilis, or a mixed form of hepatic cirrhosis with descending and obliterative cholangitis (the disease usually called congenital obliteration of the bile ducts). Lavenson supported the view that in most instances the obliteration is due to an anomaly of development and atresia of the ducts, an opinion concurred in by Holmes, and

[1] *Congenital Obliteration of the Bile Ducts*, 1892.
[2] *Jour. Med. Research*, 1908, **18**, 61 (literature).
[3] *Am. Jour. Dis. Children*, 1916, **2**, 405.
[4] *Boston Med. and Surg. Jour.*, 1922, **87**, 923.
[5] *Brit. Med. Jour.*, 1907, ii, 947.

that the associated cirrhosis is the result of the ensuing biliary stasis. Holmes, likewise, believes that the condition is usually a developmental anomaly and not primarily the result of inflammatory processes. Syphilis is not often evident, the Wassermann reaction being negative in the more recently studied cases. Feldman[1] reported a case, one of twins, the other being normal.

Clinically, the disorder is characterized by jaundice, which is present at or develops soon after birth, although rarely it may be delayed for several months; it becomes persistent and intense. The stools become acholic, if not acholic from birth; the urine contains bile pigments; the liver and the spleen are enlarged; vomiting often ensues; and hemorrhages occur from the umbilical cord and into the subcutaneous and the submucous tissues. Gradually the infant emaciates; stupor, coma, or convulsions (cholemia) develop and death ensues. The course is rarely less than a week; usually it lasts for several weeks or several months.

Diagnosis.—The more benign icterus neonatorum (which occurs in 30 to 80 per cent. of all newly-born infants on about the third day and slowly disappears) may be distinguished usually by the presence of bile in the feces and by the less-marked jaundice which soon fades. When icterus persists longer than two weeks and increases in intensity a more serious condition should be suspected. Syphilis may be excluded by the absence of a history of parental syphilis, the absence of other evidences of it, non-response to antisyphilitic treatment and by a negative Wassermann reaction. If sepsis and syphilis can be excluded and if the icterus increases in intensity, the likelihood of obstructive jaundice must be considered. Rarely a congenital jaundice persists into adolescence or adult life. This type of disorder was first studied by Minkowski,[2] and later by Chauffard[3] who, separating it from the aforementioned types, believes the essential change to be, not a radicular cholangitis, but a splenohemolysis—an anomaly in the destruction of the blood influenced by a primary disorder of the spleen.

Treatment.—Surgery offers the only hope and Holmes believes that in 16 per cent. of cases the anatomical relations indicate that operative relief is theoretically possible. Exploration should be made early, as soon as the diagnosis is reasonably certain.

INFECTIONS OF THE BILIARY TRACT

The biliary tract is particularly susceptible to, and frequently the seat of, infections. The result of these varies with the virulence of the infecting microörganism and the resistance offered by the subject: they may be insidious or frank in onset, acute, subacute, or chronic in course, and slight or extremely severe in character; or they may be entirely latent. The frank acute cholangitis and cholecystitis are usually so obtrusive as scarcely to escape recognition; when, however, the infection is more insidious in onset and subacute or chronic, and the infecting

[1] *Lancet*, 1924, ii, 113.
[2] *Verhandl. d 18th Cong. f. Inner Med.*, Wiesb., 1900, p. 316.
[3] *Semaine méd.*, 1907, **27**, 25.

microörganisms of low virulence, the resulting lesions are of such nature and the symptoms so slight, or altogether absent, that they are often ill understood, misinterpreted, and referred to other organs.

The introduction of microörganisms of low virulence into the biliary tract may be unattended by pathological lesions; this is the more likely if the ducts are patent, the flow of bile unobstructed and the bactericidal power of the liver is efficient. Comparatively virulent microörganisms may be disposed of if the biliary drainage is free and unimpeded (and the liver bactericidal function is unimpaired), but otherwise serious and even fatal forms of disease are thus provoked—suppurative cholangitis and suppurative and gangrenous cholecystitis. Between the extremes of mild and severe lesions that lead to early disaster lie the great majority of cases of biliary infection.

The immediate results of moderate or low-grade infection of the biliary tract is the production of a catarrh with the usual inflammatory phenomena—œdema and congestion of the mucous membrane, increased production of mucus, and desquamation of epithelium. If the biliary circulation is free, the results of this catarrh are washed away for the most part, but on account of special local conditions they are likely to accumulate, to become accentuated, and to persist in the gall-bladder; in the event of obstruction to the free flow of bile, these are all the more certain to occur. In many cases the lesions thus provoked are entirely latent or without noteworthy symptoms; they may pursue a short course or continue for years; and they constitute an important factor in the etiology of gall-stones. Careful microscopical, chemical and bacteriological study of duodeno-biliary aspirates will detect many of these early or latent cases (otherwise overlooked), and treatment by non-surgical drainage will cure many of them or retard the development of the later more serious pathology.

The inflammatory disorders of the biliary tract represent varying manifestations of infection; etiologically, anatomically, and clinically they have much in common; and they occur in varying relationships the one to the others—singly or combined. One infectious agent, the typhoid bacillus, for instance, may give rise to cholangitis, cholecystitis, and cholelithiasis concurrently or sequentially; one of these disorders, cholecystitis, for instance, having developed, may lead to another (cholelithiasis), and the secondary condition serves to maintain the first; acute catarrhal cholangitis may become chronic and is usually associated with gall-stones, and one or other of these conditions may lead to suppuration within the biliary tract; it is often difficult clinically to differentiate these disorders; and the diagnosis must often comprise more than one of them.

Infectious Agents.—Although considerable interest attaches to post-mortem studies of the bacteriology of infections of the biliary tract, the results are frequently vitiated by various factors, and cannot be relied upon implicitly unless the examinations are undertaken a very short time after death. The conditions at operation are quite different and the results more trustworthy—although in subsiding or long-standing infections the primary infective agent may not be recovered, since it may have died out or been overgrown by secondary invaders. Kelly

studied the bacterial cause of the infection of the biliary tract in 240 patients operated upon by John B. Deaver:

	Cases.	Per cent.
Bacillus coli communis was found in	68	28.33
Bacillus typhosus was found in	27	11.25
Staphylococcus aureus was found in	7	2.92
Streptococcus was found in	1	0.42
Staphylococcus albus was found in	2	0.83
Bacillus coli and Staphylococcus aureus were found in	2	0.83
Unidentified bacilli were found in	6	2.50
The cultures remained sterile in	127	52.92

In general these results do not differ materially from those obtained by other observers. Other bacteria have been isolated from the biliary tract, such as the cholera bacillus, *Bacillus subtilis*, *Bacillus capsulatus aërogenes*, leptothrix, etc. Biliary infections complicating pneumonia and influenza suggest the possibility of the pneumococcus and the influenza bacillus being the etiological agent. Some etiological importance attaches to anaërobic bacteria—which abound in the intestine.

By non-surgical biliary-tract drainage, it is possible to study infection of the biliary passages during life, both before and after surgery has been practised, and the cultural drainage findings compared with those recoverable directly from the gall-bladder. Granting the criticism of the accuracy of cultural recoveries from the duodenum as indicating infection of the liver, ducts and gall-bladder, nevertheless, the margin of error is not as great as commonly supposed provided the proper technique is followed. In a study of 905 biliary-tract cultures on 488 patients, Lyon found 8.6 per cent. contaminated cultures, 15.6 per cent. sterile, 23.9 per cent. mixed cultures (more than one bacterium), and 51.7 per cent. pure cultures (one bacterium only). Classifying these: the *Staphylococcus aureus* was recovered in 38.4 per cent. of positive cultures; *Bacillus coli* in 36.9 per cent.; and streptococci (hemolytic, non-hemolytic or viridans) in 22.6 per cent. The remaining 2 per cent. were made up of *Bacillus pyocyaneus*, *Bacillus typhosus*, *Bacillus lactis aërogenes*, pneumococci, diphtheroid bacilli and yeast. In those patients referred for operations from whom cultures were made directly from the gall-bladder bile, scrapings from gall-bladder mucosa, or from macerated gall-bladder tissue, the same organisms recovered by non-surgical drainage were demonstrated in the gall-bladder in the larger number of cases, and in those in whom the gall-bladder cultures remained sterile postoperative drainage study demonstrated the likelihood of infection within the liver (an infective hepatitis).

Pathways of Infection.—These are: (1) The diverticulum of Vater and the common bile duct; (2) the portal circulation; (3) the systemic circulation; (4) the lymphatic circulation; and (5) directly through the wall of the gall-bladder or the biliary ducts from the peritoneum.

1. *Infection from the duodenum by way of the diverticulum of Vater and the common bile duct* has long been looked upon as the most likely and the most common source of biliary infections, but whether with good reason remains to be decided. Although the frequency of *Bacillus coli* and *Bacillus typhosus* in infections of the biliary tract suggests an intestinal

source, these bacteria find a direct pathway from the intestine to the liver by the portal circulation. Furthermore, whereas the jejunum and the ileum always contain many bacteria, the duodenum when free from food is occasionally bacteria-free; certainly, in health its bacterial content is small and it does not contain the bacteria often found in cholangitis, cholecystitis, etc. It is quite likely, that in conditions of disease of the upper intestine, when bacteria are present in the duodenum, the biliary tract may become infected by way of the diverticulum of Vater; doubtless many of the cases of catarrhal jaundice following gastro-duodenitis arise in this fashion. In patients with acute or chronic respiratory tract disease, with gingivitis, infected tonsils, dental caries, etc., the bacterial dosage constantly swallowed may pass through the stomach and infect the duodenum, thence to ascend the common bile duct, under suitable conditions. There are two important factors opposing a ready ascending infection of the biliary tract; the one, the action of the sphincter of the diverticulum; the second, the influence of the free flow of bile. It is doubtful if infection of the biliary tract ever takes place by way of the diverticulum of Vater in the absence of stasis of the bile. One of the most important factors in preventing such infection is the free flow of the bile—the free flow rather than the bile itself, since bile is a quite favorable medium for the growth of bacteria.

2. *Infection by way of the portal circulation* is a common source of biliary infection. Definite experimental proof that the bile may become infected from the circulation was furnished years ago and there is no doubt that bacteria transported to the liver by the portal circulation may be found in the bile. Under normal circumstances bacteria carried to the liver by the portal circulation are there destroyed by the bactericidal properties of the liver cells; but there is a limit which when overcome permits the entrance of bacteria into the biliary passages. Adami having shown that under apparently normal conditions bacteria may be found in the deeper layers of the intestine, in the portal circulation, and in the liver, suggests that they invade the portal circulation through the aid of the leukocytes—which are especially active during digestion, carrying foodstuffs, foreign matters, bacteria, etc., between the epithelial cells to the lymphatic radicles and the portal venules. Ordinarily most of the bacteria are destroyed; sometimes, however, they pass through the liver and appear in the bile; in other cases they invade the general circulation. This is the latent infection of Adami and certain French and German writers.

3. *Infection by way of the systemic circulation* is probably not a very common source of infection of the biliary tract. Its importance has been enhanced since we have ascertained the frequency of bacteriemia. Doerr found that microörganisms injected into the general circulation of rabbits appear in the gall-bladder within a few hours, and that typhoid bacilli and colon bacilli multiply in the gall-bladder and may be recovered therefrom in pure culture even after four months. The occurrence of cholecystitis and cholangitis as a complication of general infections suggests the likelihood of the infection occurring by the general circulation; but one must concede the possibility of the local biliary infection

being due to organisms other than those occasioning the primary infection, and that the complicating infection may occur by the portal circulation or the diverticulum of Vater. Infection by the hepatic artery is a descending infection and operates as does infection carried by the portal circulation since both circulations commingle at the periphery of the liver lobules; but infected blood carried by the cystic artery may, although probably rarely, lead directly to infection of the gall-bladder without the intermediation of infected bile.

4. *Infection by way of the lymphatic circulation* is probably an infrequent source, although, Graham[1] has called attention to the possibilities of this mode of infection, secondary to infections in the liver.

5. *Direct infection through the wall of the gall-bladder* or of the ducts from the peritoneum has been suggested as a possibility; but excluding cases of general peritonitis in which the gall-bladder may participate secondarily and in which the mechanism of the local infection may be quite obvious, it is doubtful if infection of the biliary tract directly from the peritoneum can occur in the absence of adhesions—in which event it is probably an infection by way of the lymphatic circulation.

The pathways of biliary infection vary with the infecting agent. *Bacillus coli* infections, which must be looked upon as the most common, doubtless occur most frequently by way of the portal circulation. In most cases the liver in full functional activity is enabled to destroy or render innocuous such colon bacilli as may pass the barrier of the intestinal mucosa and be transported to it; but should the physiological activity of the liver become impaired, or should the colon bacilli become of heightened virulence, bacilli of attenuated virulence may pass over into the biliary circulation and, being excreted with the bile, set up a low-grade biliary catarrh. This commonly passes unnoticed but it is one of the most important factors in the etiology of gall-stones, as also in the complications of gall-stones. We must admit that, in the event of gastro-duodenitis, colon bacilli, as well as other bacteria, may infect the biliary passages by way of the common duct; in this event, the lesions are likely to be more abrupt in onset and more manifest clinically.

ACUTE CATARRHAL CHOLANGITIS (CATARRHAL JAUNDICE)

Etiology.—Acute catarrhal cholangitis, more commonly called jaundice, is a common disorder in young adults, although it occurs at all ages, and more common in men than in women. The disorder usually follows gastro-intestinal catarrh. Perhaps most cases follow some dietetic indiscretion or overindulgence in alcohol. These set up gastro-intestinal catarrh, which spreads to the biliary passages.

Pathology.—The lesions consist of congestion, swelling, œdema, and increased production of mucus at the lower end of the common bile duct and of the duodenal mucosa adjacent to the diverticulum of Vater. In some cases the swelling itself is sufficient to obstruct the flow of bile, but in other cases a plug of inspissated tenacious mucus effectually

[1] *Surg., Gynec., Obst.*, 1918, **26**, 394; *Arch. Surg.*, 1921, **2**, 92.

blocks the diverticulum of Vater. In many instances the plug of mucus may be recovered *en bloc* by duodeno-biliary drainage and be seen to be a firm cast of the common duct alone, or occasionally, Y-shaped mucus casts, plugging both common bile duct and the pancreatic duct of Wirsung. They may measure 1 to 6 cm. in length. The plug may extend into the hepatic ducts or into the cystic duct, obstructing them. They may most readily be dislodged by non-surgical drainage. The swelling and congestion often subside after death, so that their absence at the necropsy is not trustworthy evidence of their absence during life. All the tissues are bile-stained; rarely the liver may be swollen; the biliary ducts and perhaps the gall-bladder may be distended by bile.

Opportunities to study the lesions in catarrhal jaundice are rarely afforded, since the disease in itself is not fatal. There are many reasons, however, for believing that the cases interpreted as catarrhal jaundice are not all of one type. In many cases, doubtless, the lesions are as described; in others, perhaps, the lower end of the common bile duct, itself not diseased, is obstructed from without by catarrhal changes in the surrounding duodenal mucosa; in other cases the swelling and consequent obstruction occur perhaps higher up in the common bile duct, or in the hepatic duct, or involve the finer intrahepatic branches. It is not unlikely that many cases are as that described by Eppinger,[1] who studied the lesions in a case of catarrhal jaundice in which death occurred from accident on the eighth day. The significant lesion was hyperplasia of the lymphoid tissue of the mucosa of that part of the common biliary duct that runs in the wall of the intestine; this led to complete occlusion of the common duct and dilatation of the rest of the biliary system.

Symptoms.—In most cases the early symptoms are those of the provoking gastro-intestinal catarrh: loss of appetite, bad taste in the mouth, coated tongue, foul breath, epigastric distress especially after eating; flatulence, nausea, and perhaps vomiting; there may be constipation, or perhaps diarrhœa; and the patient complains of headache, vertigo, mental depression, general malaise, etc. Rarely there is an acute onset, jaundice being the first symptom noticed; but in most cases after the symptoms mentioned have lasted for a few days to a week, the patient becomes slightly jaundiced. The jaundice is of slow and insidious onset, and gradually increases. With its appearance, sometimes before there is any obvious jaundice, the stools become pale in color and soon are devoid of bile pigment; the urine becomes scanty, dark in color, deposits an abundant sediment, and shows the presence of bile pigments. Usually the bile pigments can be detected in the urine before the appearance of the jaundice in the sclerotics. The van den Bergh test for bilirubin in the blood serum will usually give a prompt direct reaction, although delayed direct or biphasic reactions not uncommonly appear at different periods of the illness.

When the disorder is fully developed, that is, at the end of four or five days, the jaundice is usually well marked, but even when highly developed the color is distinctly yellow, the dark olive-greenish discoloration of

[1] *Wien. klin. Wchnschr.*, 1908, **21**, 480.

malignant disease never developing. Pruritus is often marked; sometimes it precedes the development of the jaundice. The pulse usually is slowed, 60 or less per minute, and may reveal the dicrotism of low tension; sometimes this is obvious as a well-marked capillary pulsation. The patient usually is irritable or melancholic, often sleepy, and loses flesh and strength.

In most cases neither the liver nor the gall-bladder is palpably enlarged or tender; sometimes, however, the liver can be felt below the costal margin. In cases in which the liver or gall-bladder is much enlarged one should suspect a complicating cholecystitis or inflammation of the intrahepatic ducts. The spleen may be enlarged. Fever (101°) is occasionally present, but it is rarely due directly to the cholangitis, except in the epidemic infectious cases; that which sometimes occurs at the beginning of the attack and lasts a day or two is probably due to the gastro-enteritis; when conspicuous or when it lasts more than several days, it suggests some one of the types of toxic or infectious jaundice (of which, in reality, it may be a mild manifestation). Often late in the disorder the temperature is subnormal.

At the end of about a week, sometimes not until later, the evidences of gastro-intestinal irritation subside, the bad taste in the mouth and the coated tongue disappear, and the appetite returns; in some cases, however, nausea and vomiting persist for ten days or more; and in most cases constipation continues as long as the feces are clay-colored. Gradually the evidences of biliary obstruction lessen, bile pigments appear in the feces, and disappear, first from the urine and then from the skin, where, however, traces may be found for several months. Restoration of the general health is often much delayed; and may not occur until the bile pigments begin to be removed from the tissues. Ordinarily an attack lasts three or four weeks, but sometimes six weeks or more.

Diagnosis — In most cases the diagnosis is readily made from the youth of the patient (although the condition is not uncommon in older persons, and then often complicated by other evidence of liver or gall-bladder disease), an antecedent gastro-intestinal catarrh, and the absence of local pain and of serious involvement of the general health (emaciation, etc.); the diagnosis is further confirmed by the benign and favorable course, which in many cases determines the diagnosis. Doubt regarding its catarrhal nature should be awakened by the occurrence of jaundice in a middle-aged or elderly person, especially if it becomes deep or olive-tinted and if it lasts more than six weeks. Jaundice in a middle-aged or elderly person is much more likely to be due to impaction of a gall-stone, or to carcinoma compressing the common duct. In gall-stones there is usually a history of past infection of the biliary tract, or of definite attacks of cholelithiasis, and the jaundice is commonly preceded by pain; in impaction of the calculus in the common duct there are usually periodic attacks of chills, fever, and sweats, and variation in the degree of the jaundice; occasionally, however, in protracted catarrhal jaundice, fluctuations in the intensity of the jaundice occur, but these relapsing cases are usually referable to dietetic or other indiscretions. Mild grades of so-called toxic or infectious jaundice may be mistaken for catarrhal jaundice

perhaps often they are only different grades of the same process; but in infectious jaundice there is usually an acute onset with fever, and signs of general infection are more prominent—enlarged spleen and liver, albuminuria, etc.

Prognosis.—As a rule, the immediate prognosis is good; the disease of itself does not endanger life, and recovery is usually complete, but the ultimate prognosis depends upon the ability of the liver cells to react from the pressure damage and therefore bears a definite relationship to the duration of jaundice and the integrity of the liver cells or their power to regenerate. Most cases last from three to four weeks, but sometimes longer; cases lasting five months and followed by recovery have been reported, but protracted as well as relapsing cases of jaundice are usually due to other causes. So-called abortive cases of slight grade and short duration may subside entirely within two weeks or less. In cases that begin with much fever the prognosis should be guarded, since they may be the early stage of, and progress to, serious and fatal forms of jaundice. Protracted cases in middle-aged and elderly persons are sometimes of serious import—in consequence of impairment of the general nutrition and the tendency to hemorrhage. Usually complete recovery ensues, but sequels are not unknown; recurrences are not uncommon. In some cases a mild grade of chronic catarrh persists, which, involving the gall-bladder and the intrahepatic ducts, may lead to hydrops of the gall-bladder, a mild chronic cholecystitis, cholelithiasis, etc., and perhaps also to some cases of biliary cirrhosis; and from progress of the infection, to infection and chronic inflammation of the pancreas.

Treatment.—The treatment, until recently, has been essentially that of the gastro-intestinal catarrh. The patient should go to bed; for several days at least the diet should be reduced to a minimum, and should consist of a moderate amount of milk, preferably skimmed milk, or broth. The common distaste for food is a good indication to give no food whatever for a day or two, and to be content to relieve the thirst with water or the alkaline waters, but alkalis, especially sodium bicarbonate, may be added to ordinary water. Nausea and vomiting, if they persist after withdrawal of the food, may be relieved by lavage with hot water, the drinking of hot alkaline water, or the administration of bismuth subnitrate or subcarbonate, etc.; or by warm applications to the epigastrium. A knowledge of the state of gastric chemistry in the individual patient will be of prime value in selecting the type and character of medicine given by mouth. The bowels should be opened freely. Custom sanctions the use of calomel (a blue pill is equally efficacious); it should be followed by a saline aperient. These are much more efficacious if taken hot (or in hot water). They should be given in sufficient dose to cause one or two free evacuations daily; more are undesirable. The diarrhœa sometimes present in the early days of the attack rarely demands treatment. Occasionally it may be necessary to administer astringents and antifermentatives, but preparations of opium should be avoided.

After several days, when the gastro-intestinal catarrh begins to subside, the tongue to clear, and the appetite to return, additions may be made to the diet, but for some days still, only milk diluted with lime-

water or Vichy-water, thin or strained soups, milk toast or dry toast, fish, etc., should be allowed. Later one may add chicken, chops, rice and other carbohydrates, the finer green vegetables, etc.; but for some time all highly seasoned food and food likely to undergo fermentation must be avoided. The indication of progress toward liberality in diet is found not in the degree of jaundice but in the return of bile pigment to the feces and its diminution in the urine. The use of the alkaline aperients should be continued. Injections into the rectum of cold water are sometimes very efficacious in stimulating intestinal, and perhaps also gall-bladder, peristalsis. As the biliary stasis begins to subside, diluted nitro-hydrochloric acid and bitter tonics are useful. Excessive flatulence is sometimes distressing; it may be relieved by the use of bismuth salicylate, soda-mint, aromatic spirit of ammonia or chloroform water.

The pruritus is best relieved by the measures that tend to relieve the biliary catarrh and thus promote the removal of bile pigments from the tissues. Temporary relief may also be obtained by the use of cold sponging, or of a phenol lotion (1 to 40 to 60), or the internal use of the bromides or other sedatives. The general health requires attention for some time, often months, after an attack of catarrhal cholangitis.

The above outline comprises the plan of management considered orthodox for many years. Under it the duration of acute catarrhal cholangitis (catarrhal jaundice) ranges between fourteen and thirty days probably depending upon the extent of the duct catarrh, the firmness of the obstructing plug of mucus and the strength of the *vis a tergo* represented by the bile pressure from liver and gall-bladder. Lyon,[1] and later Hopkins[2] and others, have strongly advocated the use of non-surgical biliary-tract drainage, stimulating with magnesium sulphate. By this, the duration of the average case of catarrhal jaundice is decreased by more than half, thus protecting liver and pancreas cells from pressure damage. In certain more favorable cases, it has been possible to open the common duct and establish drainage and to clear all visible evidence of jaundice in as short a time as three days. The promptness with which this can be accomplished depends upon the extent to which the obstructive catarrh has ascended the common duct, but in some instances it has been possible to dislodge the larger amount of the obstructing plug of mucus within a few hours' time and to establish partial drainage, which thereafter becomes more and more rapid as the dammed-up bile in the liver aids in flushing out the ducts. In certain cases, it will be found that after the obstructive catarrh of the common duct has been removed and the inflammatory œdema has subsided, the cystic duct remains blocked for some days thereafter.

Mode of Procedure. The duodenum should be continuously irrigated by a rapid continuous drip with hot water or normal salt solution, with stimulation with 33 per cent. magnesium sulphate solution once or twice a day until the obstructing plug of mucus has been brought away intact or in pieces, and drainage has become established for several days. Then intermittent drainage can be substituted and continued until the patho-

[1] *Am. Jour. Med. Sci.*, 1920, **159**, 503.
[2] *Med. Clinics North America*, 1920, **3**, 1463.

logical objective evidence disappears or the van den Bergh reaction becomes normal. The orthodox measures of management mentioned above may, of course, be added.

Any case of acute catarrhal cholangitis that fails to respond to such management within three or four days is probably not catarrhal cholangitis, unless it involves the intrahepatic ducts alone.

SUPPURATIVE CHOLANGITIS

Etiology.—Suppurative cholangitis results from virulent bacterial infection of the biliary ducts. The common infectious agents are *B. coli*, staphylococci, streptococci, pneumococci, *B. typhosus*, *B. pyocyaneus*, the comma bacillus, *B. aërogenes capsulatus*, etc. *B. coli* is sometimes found alone, but it is not improbable that in some of the cases it is a secondary invader, or has been present in association with and has outgrown the other or primary infectious agents. *B. aërogenes capsulatus* usually invades the tissues only during or just prior to death, but occasionally it is the primary agent and may be found during life.

The infection may occur by the portal or the general systemic circulation (descending infection), or by the duodenum and the diverticulum of Vater (ascending infection). Infection sometimes occurs in certain general infections, but it is rendered much easier of accomplishment by local disease of the biliary tract; indeed, aside from very virulent infection it is doubtful if infection of the biliary tract ever occurs in the absence of local biliary disease, since the free flow of bile is usually considered an effective preventive of biliary infection. Suppurative cholangitis, however, is occasionally observed in association with general infections. The provoking microörganism, aside from the typhoid bacillus, is often not that of the primary infection, but the colon bacillus or the pyogenic cocci. This cholangitis rarely occurs without concomitant cholecystitis.

In the great majority of cases suppurative cholangitis is definitely related to local disease of the biliary tract. The local disease acts as the necessary predisposing agent; this comprises all disorders that interfere with the free and unimpeded circulation of the bile and reduce the resistance of the biliary ducts. The commonest antecedents of suppurative cholangitis are gall-stones and tumors obstructing the ducts. Gall-stones themselves are a consequence of low-grade biliary infection and catarrh, and by the obstruction to the flow of bile (stasis) that they induce, as well as because of the consequent reduction in the resistance of the biliary mucosa, they participate in the formation of a vicious circle. Suppurative cholangitis thus may supervene upon long-standing chronic catarrhal cholangitis with or without cholelithiasis, upon acute impaction of a gall-stone in the ducts, and upon chronic infective cholangitis with a gall-stone in the common duct. Tumors of the biliary ducts or of the adjacent tissues that may obstruct the ducts favor the development of suppurative cholangitis by obstructing the flow of bile and causing secondary dilatation and reduction in the resistance of the ducts, and, in the event of the growths becoming ulcerated, by affording a means of ready access for bacteria. Suppurative cholangitis of varying grades

not infrequently follows as a postoperative sequel of cholecystectomy, and even choledochostomy. In either a latent or severe form it may antedate surgery. It more commonly occurs, however, as a result of residual hepatitis.

Pathology.—The process is usually widespread. The biliary ducts are dilated (in advanced cases often enormously dilated) and filled with purulent material, commonly stained with bile. The walls of the ducts are much thickened, softened, and the seat of purulent infiltration; the mucosa is congested, œdematous, and covered with a layer of muco-pus, and in fairly well-advanced cases irregularly ulcerated. Usually analogous changes are found in the gall-bladder. About the terminal branches of the biliary ducts there are usually small abscesses; these may be very small and numerous, but in advanced cases some at least have attained considerable size, in consequence of confluence of small abscesses. The liver is enlarged, swollen, softened, and opaque; the surface usually is irregular, in consequence of the projection of many small abscesses. The cut surface shows more or less, sometimes enormously, dilated biliary ducts, filled with pus (multiple abscesses), and the intervening liver tissue shows marked periductal congestion, parenchymatous degeneration, and necrosis. The abscesses on the surface of the liver may extend to the adjacent peritoneum and set up perihepatitis or more widespread peritonitis, and perhaps extend to the pleura and the lungs or the adjacent intestine; or the process may involve the portal vein or the hepatic artery or the suppuration may extend along Wirsung's duct and induce suppurative pancreatitis and abscess in the lesser omentum. The adjacent lymphatic glands, especially those in the portal fissure, are congested, swollen, softened and sometimes necrotic.

Symptoms.—The symptoms are not always distinctive; sometimes not even suggestive. Usually there is a history of antecedent cholelithiasis or vague symptoms that may be interpreted as due to gall-stones; in other cases there is some impairment of the general health, which, in the light of subsequent events, may be ascribed to malignant disease; in still other cases the patient suffers from, or has recently suffered from, some general infection, such as typhoid fever, etc. The onset is often insidious; occasionally the first noteworthy symptom is slight jaundice, but in perhaps most cases, especially in cases in which there has been antecedent jaundice due to other causes, the onset is announced by phenomena, such as chills, fever, and sweats. These are usually severe, more or less frequently repeated at irregular intervals, and soon lead to emaciation, loss of appetite, nausea, perhaps vomiting, diarrhœa, etc.; variable afebrile periods, however, are not uncommon. Jaundice is almost always present but it is variable in degree; usually it is slight or moderate only, except in cases when the cholangitis is associated with other conditions that cause intense jaundice. Rare cases of suppurative cholangitis without jaundice have been described.

Sometimes there is no pain in the region of the liver. Usually there is at least dull aching or discomfort (tension of the liver capsule); now and then there is more severe pain due to acute cholecystitis, cholelithiasis, perihepatitis, peritonitis, etc. The liver is enlarged and usually

continues to enlarge. It presents a smooth surface, except in the event of an unusually large abscess presenting on the palpable surface, and it is tender; perhaps, also, there may be a tender spot posteriorly on the right side on a level with and 2 to 3 cm. from the twelfth thoracic vertebra (Boas). Usually the gall-bladder is enlarged and tender (acute cholecystitis). The spleen also may be enlarged. There is a polymorphonuclear leukocytosis, more marked during and just after the febrile periods; sometimes it is absent during the afebrile periods.

Extension of the lesions locally may lead to the ordinary signs of local or general peritonitis, pleuritis, etc., with perhaps evacuation of pus through a bronchus. Absorption of toxins may induce severe headache, joint pains, swelling, and tenderness, and their excretion may be attended by albuminuria and casts. Involvement of the hepatic vein may lead to multiple abscesses in the lungs, infectious endocarditis, general septicopyemia, etc. Sometimes a single abscess ensues, and may establish communication with the intestine or pleura and lung.

Diagnosis.—This is usually apparent from a history of antecedent gall-stones or other disorder of the biliary tract, or of typhoid fever or other infection, and the development of chills, fever, and sweats, and jaundice, local pain, progressive enlargement of the liver, perhaps also of the gall-bladder and spleen, and leukocytosis. In the absence of a history of antecedent disease of the biliary tract, the other symptoms mentioned, if at all outspoken, suffice for the diagnosis; but in many cases the symptoms are added so insidiously to those of the antecedent disease, or they are, in the beginning at least, so mild and evanescent, that it is difficult if not impossible to say just when the suppurative process began or how severe it is. A slight and temporarily increased obstruction to the flow of bile may lead to increased absorption of toxins from a chronically infected biliary tract and increase of the general and local symptoms; release of the obstruction may permit of the free discharge of pus from the biliary tract with subsidence of the symptoms. Thus in some cases recurrences and remissions of the symptoms occur, for instance in the discharge of an impacting gall-stone, drainage may become very free and lead to temporary subsidence of the symptoms.

Difficulty may be experienced in differentiating suppurative pylephlebitis, other forms of abscess (especially solitary or tropical abscess), malaria, etc. Jaundice is not an essential symptom, but it is suggestive of and occurs earlier in suppurative cholangitis than in pylephlebitis or single abscess of the liver. Enlargement of the spleen, while it occurs in suppurative cholangitis and pylephlebitis, is more common in pylephlebitis; but cholangitis and pylephlebitis may coexist. In abscess there is usually a history of dysentery. Malaria may be excluded by the absence of plasmodia from the blood, and the leukocytosis.

Prognosis.—This is decidedly unfavorable, but it is modified by a number of attending phenomena and the treatment. In view of the difficulty of determining accurately the time of onset, it is difficult to say how long it lasts; but the acute cases which pursue a progressive course seldom continue more than three weeks. In less severe cases,

in which the infection is less virulent and becomes subacute or chronic, or in which the lesions gradually subside and perhaps become localized to the gall-bladder, or in which a fistulous communication is established and the pus is discharged, etc., the duration may be much longer and recovery may ensue. The prognosis is materially improved by the spontaneous or operative removal of the source of obstruction (gall-stones, etc.) and the consequent free drainage.

Treatment.—Prevention is much more readily effected than cure. Even minor grades of biliary infection, such as the acute and more chronic catarrhal cholangitis (jaundice), gall-stones, etc., should be carefully and persistently treated. This, especially in the event of gall-stones, comprises surgical intervention—which not only is curative of the gall-stones and the accompanying catarrh, but preventive of the more serious suppurative cholangitis. When suppurative cholangitis has developed, the treatment is essentially surgical, and consists in free drainage. Medical treatment consists in the use of salicylates, hexamethylenamine, bile salts and other remedies to disinfect the biliary tract and promote the free flow of bile. Otherwise, medical treatment is purely palliative and analogous to that laid down for acute catarrhal jaundice.

Lyon has urged a trial of non-surgical drainage of the biliary tract in cholangitis of varying grades, especially when occurring as a sequel of biliary-tract surgery. He believes that maximum drainage of the bile ducts and liver can be obtained by the duodenal drainage, three times the amount generally secured by surgical drainage of the common duct, avoidance of surgical trauma to ducts (postoperative stricture, or dilatation, etc.); avoidance of surgical shock, etc. Excellent results have followed this treatment.

CHRONIC CATARRHAL CHOLANGITIS

Etiology.—Chronic catarrhal cholangitis may involve only the larger especially the extrahepatic, ducts, or more or less of the entire biliary tract, or it may be confined to the finer intrahepatic ducts (radicular cholangitis or angiocholitis). Usually the lesions are widespread, involving the larger extrahepatic ducts, more or less of the larger intrahepatic ducts, and the gall-bladder. This form of the disease is due to the factors that provoke acute catarrhal cholangitis, and may result from repeated attacks of acute catarrhal cholangitis or from chronic low-grade infections. It is most commonly found in association with gall-stones, with which its etiology and pathogenesis are intimately associated; but chronic non-calculous cholangitis also occurs with chronic gastro-duodenal catarrh, after certain infections, with chronic obstruction, and with certain chronic disorders of the liver, such as hydatid cysts, hepatitis, chronic abscesses, etc. Chronic catarrhal radicular cholangitis or angiocholitis is rarely an independent affection.

Pathology.—The lesions consist of congestion and swelling of the mucosa, increased production of mucus, round-cell infiltration, and proliferation of the submucosa and muscularis, with the production of new fibrous connective tissue; these lead to thickening and induration of the walls of the ducts and to pericholangitis. There may be partial

or complete obstruction of the ducts. In the event of complete obstruction, the ducts become enormously dilated (up to the size of a thumb or larger); the gall-bladder and some of the intrahepatic ducts also become dilated. The biliary tract usually contains a clear, almost colorless, often sterile mucus; when the mucus is sterile, the mucosa of the biliary tract is usually quite smooth. In the event of incomplete obstruction the ducts and especially the gall-bladder are less dilated, the contents are usually turbid and often contain bacteria, and the mucosa may be more or less ulcerated.

Symptoms.—The symptoms are those of chronic relapsing jaundice. Rarely this may represent a direct continuation of an acute catarrhal jaundice, being more insidious in onset, and subject to exacerbations and remissions. The attending phenomena are those of acute catarrhal cholangitis—prolonged. In the cases of complete obstruction, if the contents of the biliary tract are sterile, there is usually no fever, and remissions in the jaundice are slight. In the cases of incomplete obstruction, remissions in the jaundice are more marked, and the biliary tract being infected, chills, fever, and sweats are common. These attacks by no means warrant a diagnosis of suppuration of the biliary tract, although they are evidences of infection. This chronic catarrhal cholangitis may lead to suppurative cholangitis (of which it is often only a minor manifestation), acute infectious jaundice, acute yellow atrophy of the liver, etc.

Diagnosis.—In cases of persisting jaundice that begin seemingly as acute catarrhal cholangitis, one must attempt to eliminate cholelithiasis and malignant disease obstructing the ducts. Often it is quite impossible to differentiate non-calculous from calculous cholangitis with a gall-stone in the common duct. A history of antecedent gall-stone colic is suggestive but by no means conclusive. Hypertrophic biliary cirrhosis may be eliminated by the absence of marked enlargement of the liver and spleen.

Prognosis.—This is dependent upon the associated lesions.

Treatment.—The treatment is essentially that of acute catarrhal cholangitis. In protracted cases operation should be undertaken with a view to drain the biliary ducts, and exclude the possibility of obstruction due to gall-stone. Non-surgical drainage, instituted early and energetically carried out, will often be successful and obviate the necessity for surgical interference.

ACUTE CHOLECYSTITIS[1]

Etiology.—It is largely artifice that leads to a distinction between cholangitis and cholecystitis; the one like the other is an expression of

[1] The current literature on this subject and chronic cholecystitis is voluminous. Among the more valuable recent articles are: Peterman, Priest and Graham, *Arch. Surg.*, 1921, **2**, 92; Graham, R. R., *Arch. Surg.*, 1921, **3**, 154; Erdmann, J. F., *Surg. Clin. North Am.*, 1921, **1**, 279; Chiray and Semelaigne, *Presse Med.*, 1922, **30**, 685; Graham and Peterman, *Arch. Surg.*, 1922, **4**, 23; Deaver and Reimann, *Surg. Clin. North Am.*, 1922, **2**, 35; Hurst, A. F., *Practitioner*, 1923, **111**, 321; Peterman, M. G., *Surg., Gynec., Obst.*, 1923, **36**, 522; Nordmann, O., *Arch. f. klin. Chir.*, 1923, **127**, 600; Westphal, L., *Ztschr. für klin. Med.*, 1923, **9**, 22; Mayo, W. J., *Ill. Med. Jour.*, 1924, **45**, 33; Gundermann, W., *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1924, **37**, 781; Heyd, Killian and MacNeal, *The Beaumont Lectures*, St. Louis, C. V. Mosby Co., 1924; Mayo, C. H., *Ann. Surg.*, 1925, **81**, 955; Tanner, W. E., *Guy's Hosp. Rep.*, 1925, **75**, 170.

infection of the biliary tract. In some cases the infection may remain confined to the ducts or the gall-bladder. In other cases, developing in the one or the other, the process may extend to that not primarily involved; and it may persist in the gall-bladder and subside in the ducts, or *vice versa*. A separate discussion of the two conditions seems warranted, however, because cholecystitis is characterized by certain definite features that develop largely because the gall-bladder is a closed sac with a small and readily obstructed exit, and because a common sequence of cholecystitis is cholelithiasis, which serves to keep active or readily induces cholecystitis.

Like cholangitis, cholecystitis results from bacterial infection, which is facilitated by any cause that reduces the resisting power of the gall-bladder or interferes with the free flow of bile. Mixed infections are not uncommon; and in some cases one organism having set up the lesions may die out spontaneously or be overgrown by another, whence in some cases the gall-bladder contents are sterile or the primary infectious agent eludes detection. The infectious agents reach the gall-bladder usually by way of the portal circulation or the general systemic circulation, although, of course, they may reach it by way of the diverticulum of Vater and the common bile duct. When cholecystitis or cholangitis complicates typhoid fever, pyococcic infections, etc., a natural inference is that the microörganismal cause of the general or primary infection is the cause of the local complication in the biliary tract – an inference usually but not always borne out by the fact. A biliary infection complicating or occurring sequentially to pneumonia, influenza, etc., may be due not to the specific cause of the general infection, but to pyogenic cocci or the colon bacillus, the original infectious agent or its toxin perhaps having prepared the way for the secondary invader. Certain parasites (especially round-worms, bilharzia) may invade the biliary tract, and set up cholecystitis; in some cases, however, they act only as the carrier of other infectious agents.

Typhoid Infections.—At one time major interest was concerned with typhoid infections of the biliary tract but since typhoid fever has become less prevalent, other bacteria (the pyogenic cocci and *Bacillus coli*), are of much greater importance.[1] It is definitely known: (1) That the typhoid bacillus is regularly present in the gall-bladder, and commonly in pure culture, in practically all cases of typhoid fever; (2) that the typhoid bacillus may persist in the gall-bladder, as well as within gall-stones, years after the patient has recovered from an attack of typhoid fever; (3) that cholangitis and cholecystitis occur as complications of typhoid fever; and (4) that a history of antecedent typhoid fever may be obtained in many patients with cholecystitis and cholelithiasis. The manifestations are various:

1. *Acute cholecystitis* during the course of or after typhoid fever does not vary materially from acute cholecystitis due to other bacterial causes, although less likely to become suppurative.
2. The development of *gall-stones*.

[1] Consult Lyon, Bartle and Ellison: *Am. Jour. Med. Sci.*, 1922, **163**, 60 and 223.

3. *Primary typhoid cholecystitis*, often associated with cholangitis; that is, an infection of the biliary tract with *Bacillus typhosus* without other evidence of past or present typhoid infection.

4. *Chronic Carriers.*—In many cases the typhoid bacillus may be recovered from the gall-bladder years after an attack of typhoid fever.

Although bacterial infection is the essential factor in provoking acute cholecystitis, other factors are of contributing or predisposing importance; these are such as (1) reduce the vitality and resisting power of the gall-bladder and biliary ducts, and (2) interfere with the free flow of bile. Among the first mentioned are: trauma, such as blows and other injuries in the region of the gall-bladder, which rarely may reduce the resistance of the gall-bladder, and render it vulnerable to bacteria already present or that may be brought thither; a previous attack of cholecystitis and gall-stones, which favor infection; local diseases of the intestinal tract which may act as the source of the bacteria; and general disorders, such as nephritis, in which complicating or terminal infections are common. Among the conditions that act as predisposing causes by interfering with the free flow of bile are gall-stones, usually with chronic cholangitis, tumors or foreign bodies (worms, etc.) or catarrh within the ducts, especially the cystic, tumors without the ducts, kinks or cicatrices compressing the ducts, etc.

Pathology.—Various types of acute cholecystitis may be differentiated —catarrhal, suppurative, phlegmonous, gangrenous, and membranous. These are varying manifestations of the one process (an infection) which result from variations in the virulence of the infecting agent, in the resistance and in the freedom of the circulation of the bile; they differ in degree rather than in nature, and may pass almost imperceptibly the one into the others. In the mild grade of inflammation, so-called *acute catarrhal cholecystitis*, the gall-bladder is distended and tense; the wall is swollen, œdematous, and softened, and the mucosa is congested and covered with a layer of mucus. In many cases the inflammatory phenomena invade also the peritoneal covering, which then is covered with a thin layer of fibrin which may unite the gall-bladder to adjacent structures. The cystic duct usually is partially obstructed from swelling of the mucosa; sometimes it is completely obstructed, but usually only in the event of recurrent attacks of inflammation or of cicatrization of ulcerations. The contents of the gall-bladder usually consist of turbid bile; usually this is in excess and much thickened, inspissated, and not infrequently tar-like; sometimes the contents consist of turbid, bile-stained, serous, or serofibrinous fluid; rarely it may be stained with blood, in which event there is likely to be some erosion or superficial ulceration of the mucosa. Gall-stones may be encountered, especially in recurrent attacks; usually not in cases of less than four to six months' duration.

In the more severe, or *suppurative cholecystitis*, or acute empyema, the gall-bladder varies in size depending upon antecedent conditions. Should it have been previously normal or only slightly diseased and non-adherent, it may become considerably, sometimes very much, enlarged; but if previously the seat of cicatrization from chronic inflammation, no enlargement may occur; in this case it is usually united to

adjacent tissues and organs by adhesions. The wall of the gall-bladder is softened, swollen, œdematous, congested, and usually very dark reddish, greenish, or blackish in color. The mucosa is congested and desquamated, and covered with a fibrinopurulent, sometimes also hemorrhagic, exudation. In many cases there is more or less ulceration, especially toward the fundus, in consequence of the relatively poorer vascular supply of the fundus and the gravitation of gall-stones. The ulceration may proceed through the wall and lead to perforation. The cystic duct is usually occluded even in the absence of gall-stones. The contents consist of turbid, bile-stained, fibrinopurulent, sometimes sanguinolent fluid; gall-stones are present in from 60 to 80 per cent.

In some cases the phenomena are less acute; the congestion and softening of the wall are less marked or entirely absent, the wall then being thickened and indurated; there is little if any pericholecystitic fibrinous exudation, although the gall-bladder may be firmly united to adjacent organs; the mucosa of the gall-bladder is more or less ulcerated and the contents are more or less purulent—cases of so-called *chronic empyema of the gall-bladder* or *chronic ulcerative cholecystitis*. On the other hand rarely the lesions may be more acute than in the more common cases of acute suppurative cholecystitis; the œdematous, hemorrhagic, and purulent infiltration of the gall-bladder is widespread, and may lead to extensive dissection of the different coats, or extensive sloughing with or without perforation—so-called *phlegmonous cholecystitis*. A more advanced and rare stage is spoken of as *gangrenous cholecystitis*, a term very inconsiderately employed. The small foci of necrosis that occur in suppurative cholecystitis, for instance, are sometimes spoken of as localized gangrene—ulcerative cholecystitis being a more preferable term. When, however, a large section of the gall-bladder becomes necrotic the term gangrenous cholecystitis is proper. This results from very virulent infection, or interference with the blood supply due to a gall-stone impacted in the neck of the gall-bladder or in the cystic duct, or to infectious thrombosis of the nutrient artery. The lesions resemble those of advanced suppurative or phlegmonous cholecystitis, with the addition of complete necrosis or gangrene of a variable portion of the gall-bladder; the gangrene usually begins at or near the fundus (where the blood supply is poorest) and spreads toward the neck; in some cases it begins about a gall-stone embedded in the wall of the gall-bladder. *Membranous cholecystitis* is a rare condition characterized by the formation of a membranous or fibrinous coat of the interior of the gall-bladder, and perhaps of the biliary ducts. It is usually associated with gall-stones, and with mucous enteritis or colitis.

Symptoms and Physical Findings.—Acute cholecystitis is extremely variable in its symptomatology. In a few cases it is altogether latent; in other cases, although it occasions obvious symptoms, the true nature of these is often masked, and they escape correct interpretation, being commonly regarded as indigestion. Thus there are: (1) Cases in which a noteworthy enlargement of the gall-bladder occurs; but the biliary ducts being patent, the drainage sufficient, and the patient's sensibilities somewhat obtunded, there is no complaint and the disorder escapes

recognition, unless examination of the gall-bladder region shows a more or less enlarged and tender gall-bladder, It is surprising how frequently this condition occurs and how frequently it goes undetected, unless investigated by the bile drainage method and the cholecystogram method of Graham. These data added to a doubtful history and relatively negative physical examination rarely fail in making the diagnosis. (2) There are cases in which a little epigastric discomfort, perhaps slight nausea, in some cases actual pain, is complained of, and examination reveals an enlarged and tender gall-bladder. (3) Cases in which, announced by the ordinary symptoms, acute cholecystitis or cholangitis develops.

Initial nausea and vomiting, fever, pain, and tenderness in the region of the gall-bladder, rigidity of the overlying abdominal muscles, and an (occasionally) enlarged and tender gall-bladder constitute the important clinical manifestations of acute cholecystitis. These may be of sudden or rather insidious onset. The nausea and vomiting are usually moderate and soon subside, except in the event of pericholecystitis or more general peritonitis and paresis of the intestine. In catarrhal cholecystitis the fever is slight and lasts only a short time; in the cases complicating some general infection there may be little if any added fever, but if occurring during convalescence from typhoid fever, the onset of the cholecystitis is usually announced by fever, which may be high. The *pain* usually occurs first in the epigastrium sometimes directly in the mid-line, and later becomes more localized to the right hypochondrium; it varies much in character. In some cases it is dull and aching; in other cases it is sharper and more severe, and while continuous is subject to acute exacerbations; in perhaps the majority it is severe and paroxysmal and resembles the pain of so-called gall-stone colic. The complaint of pain is much influenced by the mental state of the patient: in acute infections attended by mental torpor there may be little or no complaint of pain, but there may be considerable local tenderness. The pain may be referred to the region of the right scapula, as in gall-stone colic, or to the right shoulder when the peritoneum is involved, or downward to the right lower abdominal quadrant, and suggest appendicitis, or more rarely to the left scapula (adhesions to duodenum or pylorus?); cholecystitis, appendicitis and duodenal ulcer or duodenitis may be concurrent.

There is more or less tenderness in the right upper abdominal quadrant. At first this may be diffuse, but usually it soon becomes localized to the region of the gall-bladder. The overlying muscles are rigid, and in consequence sometimes simulate a tumor of the gall-bladder. In some cases by careful palpation one can feel an enlarged and tender gall-bladder; in some cases it is also visible. However, a gall-bladder is far too frequently *mentally* rather than actually felt. The number of operations in which the gall-bladder is found of normal size, or even small, and tucked behind the overhanging edge of the liver should teach us caution in too readily saying that the gall-bladder can be easily palpated. The thickness of the abdominal wall, the rigidity of the muscles, etc., are common factors of interference. Courvoisier's law, that the gall-bladder becomes palpably enlarged in obstruction due to new growth but not to stone, is not always accurate. The degree of enlargement varies considerably

in recent cases in which the gall-bladder is non-adherent and there is little pericholecystic exudation. The tumor, corresponding with the enlargement of the gall-bladder, is pear-shaped, tense or semifluctuating, moves with respiration, and is displaceable by palpation, although both of these may be inhibited by pain; in older or recurrent cases, when there are old adhesions, and in cases in which there is considerable pericholecystitic serofibrinous and other exudation, and perhaps also involvement of adjacent tissues (with intestinal paralysis, tympanites, abscess formation, etc.), the tumor mass is likely to be more globular or irregular, or ill-defined, and it may not move at all on respiration or be movable on palpation. Usually the mass is in the region of the gall-bladder, and as it increases in size it advances toward the umbilicus; but in a considerable number of cases it descends in the flank; sometimes it is so low as to suggest periappendicular suppuration. With the progress of the disease the tumor often can be observed gradually to increase in size. As the inflammatory phenomena subside and the cystic duct again becomes patulous, the tumor decreases in size and may ultimately disappear. Some local tenderness especially on deep thumb palpation, or to the ulnar concussion test, may remain for some days or weeks. Bahrdt[1] called attention to cases masquerading as bronchitis, in which the symptoms point to the lungs and bronchi. Slight dulness with rales, fever and later slight jaundice characterize the attacks which may be numerous.

Jaundice is not a part of uncomplicated cholecystitis; its development signifies extension of the inflammation to the ducts (cholangitis), spasm of ducts, or some complication such as gall-stones obstructing or compressing the hepatic or the common duct. The liver is not enlarged unless there is cholangitis or associated hepatic cirrhosis. The pulse may be normal or slightly accelerated. Usually there is a moderate leukocytosis (12,000 to 15,000).

The *consequences* of acute cholecystitis are many and various, and of much clinical importance. In the majority of cases, especially in those occurring during general infections, the manifestations subside at the end of four or five to ten or fourteen days; perhaps in some of these cases the lesions also subside and the gall-bladder returns to a normal condition. In the great majority of cases the lesions become chronic, the infection becomes latent for a time and of minor grade: the usual consequence of this is gall-stone formation; but chronic cholecystitis may ensue without gall-stone formation. In many cases after the formation of the gall-stones the infection gradually dies out, and the gall-stones may remain latent, perhaps throughout life, although the gall-bladder in such circumstances is disposed to ready reinfection. Sometimes, especially if the infection was slight in grade and soon died out, and if a gall-stone obstructed the cystic duct or the exit of the inflammatory exudation was otherwise prevented, the contents of the gall-bladder take on a serous or mucous character, and cystic distention or hydrops of the gall-bladder results. Here the gall-bladder becomes more readily palpable, because more distended. In other cases the gall-bladder remains continuously

[1] *Munchen med. Wchnschr.*, 1912, **59**, 2326.

infected; in other cases the patient may suffer from minor phenomena due to chronic cholecystitis and in addition become subject to repeated recurring attacks of acute cholecystitis (reinfections or exacerbations of a chronic infection); in either case the lesions may become suppurative or ulcerative—so-called chronic *empyema* of the gall-bladder. Again, although the lesions of the gall-bladder subside, adhesions have developed between the gall-bladder and adjacent organs. In some cases of acute cholecystitis the lesions do not subside; they progress to the more serious forms of the disease; but suppurative phlegmonous and gangrenous cholecystitis may develop suddenly, as a primary manifestation of an infection; in about 60 to 80 per cent. of the cases they occur in connection with gall-stones, therefore in chronic infections or reinfections. The clinical manifestations consist of an aggravation of the symptoms of acute cholecystitis. The evidences of local inflammation, peritonitis, are more severe; in some cases persistent nausea, vomiting, widespread abdominal pain and tenderness, tympanites, constipation, etc., suggest general peritonitis. Occasionally the manifestations are those of acute rapidly developing general peritonitis without localizing symptoms. The gall-bladder, as a rule, is palpable—near the tip of the ninth costal cartilage in case it is incapable of little if any distention, or near the umbilicus, in the flank, or in the right inguinal region if it becomes much distended. In many cases it is quite low, being associated with cholelithiasis and linguiform lobulation (Riedel's lobe), and may simulate appendicitis. Jaundice is not a necessary symptom, but it occurs more frequently in the severer than in the milder form of acute cholecystitis, because of the associated lesions, such as gall-stones and tumors obstructing the ducts, and the more common occurrence of cholangitis. The temperature is usually high (103° to 104° F.), and commonly accompanied by chills and sweats; but in some cases of severe infection, with minor resistance of the patient, the temperature may be lower. The pulse is accelerated, 120 or more—which is a better indication of the seriousness of the condition than the temperature. Usually there is a polymorphonuclear leukocytosis of from 15,000 to 35,000 or more.

Perforation of the gall-bladder may occur: into preformed adhesions, and lead to the development of a localized abscess, which, if the adhesions involve the abdominal wall, may cause local œdema and other signs of inflammation; into the liver, and lead to a liver abscess; over the liver, and lead to perihepatitis, subdiaphragmatic abscess or pleural effusion; into the general peritoneum, and lead to widespread purulent peritonitis; into the hollow abdominal viscera, and lead to fistulæ, etc. Sometimes the onset of the perforation is announced by sudden increase of the local pain, more or less collapse, increased pulse-rate, and progression of the general symptoms; but the symptoms often only steadily increase, and no time can be set as that of the occurrence of perforation.

Diagnosis.—The diagnosis of acute cholecystitis presents no serious difficulties in the great majority of cases: nausea and vomiting, pain and tenderness in the region of the gall-bladder, rigidity of the overlying abdominal muscles, and an enlarged and tender gall-bladder constitute a complex of symptoms that can scarcely be attributed to anything else.

In some cases the symptoms are not obtrusive, and the enlarged and tender gall-bladder must be sought, but even these cases present no diagnostic difficulties. The phenomena of gall-stone colic also are properly attributable to an acute (perhaps acute exacerbation of a chronic) cholecystitis, and the local pain and tenderness and rigidity of the overlying muscles, if sought, will usually be found. The more serious forms of cholecystitis are to be distinguished from the milder or catarrhal form, usually by their more abrupt onset, or abrupt increase in severity, and by the more marked local and general symptoms, that is, more evident and perhaps widespread peritonitis and more serious toxemia, and by the fact that in most cases there is a history of antecedent cholecystitis or cholelithiasis. The onset of perforation or gangrene can rarely be diagnosed with certainty, except perhaps by a sudden increase in abdominal pain, with collapse, increased pulse rate, and spreading peritonitis; it should be suspected in the event of sudden fulminating peritonitis occurring in a chronic cholecystitic or cholelithitic subject, especially if the lesions began in or remain limited to the upper abdomen. In this event one must exclude other causes of peritonitis, in which a study of the patient's past history is of the utmost importance.

Difficulty may be experienced in differentiating acute *appendicitis*, particularly in those cases in which the enlarged gall-bladder is unusually low and perhaps projects into or is situated in the right iliac fossa; but cholecystitis is suggested by previous attacks of so-called dyspepsia or of more obtrusive symptoms of cholelithiasis or cholecystitis, especially if associated with jaundice, by relationship of the attacks to dietetic indiscretions, by limitation of the pain to the epigastrium or the right hypochondrium and radiation to the right shoulder (the pain is rarely as diffuse as is often the case in early appendicitis), by the presence of a zone of cutaneous hyperalgesia (Head) about the upper right half of the abdomen, by the fact that the mass (enlarged gall-bladder) often moves with the liver during the phases of respiration, etc. Careful examination of bile aspirates obtained by duodenal drainage will often — almost invariably — give evidence of an inflammatory condition involving the biliary tract system.

Prognosis.—In the majority of cases the prognosis in acute cholecystitis is good, the process tending to subside, under appropriate treatment, within ten days or a fortnight; the mildest cases may subside within four or five days or a week; the inflammatory and retained secretions are discharged through the cystic duct and the gall-bladder reverts to its normal size. Sequels, especially gall-stones and adhesions, however, are almost certain to occur, so that the subsequent outlook is not the best; in other cases a low-grade infection may persist and the patient become a subject of chronic infection and recurring attacks of cholecystitis. In the more severe forms, suppurative, phlegmonous, and gangrenous cholecystitis, the tendency toward spontaneous cure is slight. In this event the prognosis is grave, since not only are the lesions serious in themselves but a localized or general peritonitis may ensue and a fatal issue result, unless recourse is had to surgical intervention. Occasionally in these serious cases the obstruction of the cystic duct may be due only

to swelling of the mucosa; in this event it may lessen, and part, at least, of the contents of the gall-bladder may be discharged; but if the acute inflammatory lesions subside, chronic empyema is likely to ensue. In some cases the infection is so virulent that extensive phlegmonous inflammation or gangrene develops before limiting adhesions can form. The prognosis in these cases is extremely grave, death usually resulting unless the patient is operated upon.

Treatment.—This in general is that recommended for gall-stone colic, which virtually is an attack of more or less acute cholecystitis. The food should be reduced to a minimum; perhaps withheld altogether for a day or two, if the patient's general condition permits. Until the acute phenomena subside the diet should be bland and easily digested: milk and Vichy or lime-water, broth, cereals, etc. The bowels should be opened by enemas of hot water for the first day or two, whereupon Carlsbad salts or sodium phosphate or similar salts in hot water should be given. It is wise to withhold morphine, which, unless required to mitigate acute suffering, tends to mask symptoms, to promote a false security, and is otherwise objectionable. Relief from pain usually follows hot fomentations to the region of the bladder, lavage of the stomach with hot alkaline water, a full hot bath, etc.; if not, a small dose of morphine ($\frac{1}{16}$ to $\frac{1}{32}$ grain) may be tried; a very small dose is often extremely efficacious. Nausea and vomiting depend upon the same factors as the pain, and they usually subside with the pain.

Except in the suppurative, gangrenous or empyemic forms of acute cholecystitis, one of the most practical procedures, not only for the relief of pain, but to encourage the subsidence of the acute phenomena, is to establish bile drainage by intraduodenal stimulation with magnesium sulphate. The intermittent method should be used. Often immediate relief of pain with a drop in temperature and leukocyte count will be secured by one drainage, and a grave situation transformed into a more favorable one, when operative methods can be used with less risk.

Following subsidence of the acute phenomena the treatment recommended for cholelithiasis should be instituted.

Happily most cases of acute cholecystitis gradually subside; occasionally the local symptoms increase, evidences of more or less extensive peritoneal irritation or actual peritonitis supervene, the temperature, leukocytosis, and other manifestations of infection increase; the local lesions have progressed to suppuration, necrosis, or gangrene. In this event the necessity of operative intervention must be considered.

CHRONIC CHOLECYSTITIS

Etiology.—Chronic cholecystitis may be the residual manifestation of an acute cholecystitis, or may be chronic from the beginning. Its etiology is that of acute cholecystitis, the chronicity of the process being a manifestation of lingering infection, or the consequence of very low-grade infection with insufficient biliary drainage. In the great majority of cases the condition is associated with gall-stones, that is, most cases are

calculous cholecystitis; in a few cases the lesions extend throughout the biliary tract; that is, cholangitis and cholecystitis are associated.

Pathology.—The process may or may not be associated with gall-stones. In absence of gall-stones the lesions may be catarrhal, that is virtually confined to the mucosa, which shows more or less congestion, swelling, desquamation, and increased formation of mucus; the gall-bladder usually is distended and filled with thick tenacious bile or bile and mucus. In some cases the mucosa is thinned and atrophic, especially in spots, evidently the consequence of past erosion or ulceration. In many cases of long standing the gall-bladder becomes reduced in size, very small, and sclerotic; it may be represented by a mass of thickened contracted connective tissue, perhaps tightly enclosing one or more gall-stones, but sometimes not. When thus small and shrivelled, the gall-bladder, whether containing gall-stones or not, often makes up part of a mass of firm adhesions that bind together the adjacent tissues; in many cases the gall-bladder can scarcely be identified as such. The cystic duct is often, perhaps usually, patulous, but it may be partially or completely obstructed. In some cases the tissue adjacent to the gall-stones, or, in their absence, that lining the still-persisting lumen, is made up largely of cicatrizing granulation tissue, and may reveal no vestige of mucosa; in other cases the lining epithelium has invaded the deeper layers of the walls and is clearly hyperplastic and irregularly proliferated (beginning carcinoma). The musculature is usually atrophic, and replaced by fibrous connective tissue.

Symptoms and Diagnosis.—These are of cholelithiasis which is the important concomitant of chronic cholecystitis. The clinical differentiation between cholecystitis with and without cholelithiasis may be attempted, but those with most experience often find it difficult to determine whether or not gall-stones are present in individual cases. In some cases, it is practically impossible to say definitely whether or not gall-stones are present. The likelihood of their being present is enhanced by repeated attacks of severe colic followed by jaundice, but colicky pains are present in many cases (70.6 per cent.) without gall-stones, and jaundice may occur in 35.3 per cent. of cases without gall-stones. The detection of faceted gall-stones in the stools suggests the presence of others in the gall-bladder or ducts.

Recent methods of diagnosis have increased our ability to make such a differentiation. Generally speaking, it is more common to find a high gastric acidity in cholecystitis without gall-stones and a lower, or absent, gastric acidity in cholelithiasis. Fractional methods of testing should be used. Furthermore, the "B" fraction recovered by biliary drainage in cholecystitis is apt to be darker in color than that in cholelithiasis in which the concentrating ability (Rous and McMaster) of the gall-bladder is often greatly lessened. In cholelithiasis an excess of microscopic crystals or even gall-sand may be found. Neither of these findings, however, is to be considered a hard and fast diagnostic differentiation.

The better development of roentgen-ray methods has greatly contributed to the recognition of the pathological gall-bladder and of chronic

cholecystitis with or without gall-stones. The use of the Bucky diaphragm more readily visualizes the opacity of gall-bladders with thickened and fibrotic walls, and brings into sharper relief the denser opacities of some gall-stones which may show clearly; in others, ring-like peripheries and hollow cavities are noted, in others negative shadows.[1] Manges states, "It is probably safe to say that positive shadows of gall-stones can be demonstrated in at least 50 per cent. of cases with proper roentgen-ray technique."

The cholecystographic method, introduced by Graham,[2] using phenoltetrabromphthalein or phenoltetraiodophthalein intravenously, or by salol (or otherwise) hardened pills by mouth, has definitely increased our ability to detect the pathological gall-bladder. Graham states, and his work has been extensively confirmed, that the normal gall-bladder will fill with the dye and become readily visible within five to twelve hours after the use of the dye, the shadow will reach maximum concentration between eight and eighteen hours, and the gall-bladder will then gradually empty and be no longer visible in from twenty-four to thirty hours. Inability of the gall-bladder to fill with the opaque bile or to show evidence of proper contractibility or delayed emptying is believed to indicate a pathological gall-bladder or an obstructed cystic duct or both.

The Prognosis and Treatment.—The prognosis and treatment are the same as in cholelithiasis. In the event that surgery becomes definitely indicated in patients in whom the operative risk is not above the average, some authors believe that it is good surgical judgment to leave the gall-bladder *when possible* rather than to remove it as a routine, when preliminary medical drainage and a cholecystogram have shown that the gall-bladder retains a reasonable degree of function; and that removal of the gall-bladder should be limited to those found to have such firm adhesions, the releasing of which alone does not indicate the likelihood of restoration of proper function of the gall-bladder. These include the markedly atrophied or fibrotic gall-bladder often found contracted around a solitary stone, the dilated, atonic gall-bladder with paper-thin walls and a destroyed musculature, the gall-bladders showing mucosal pathology of the true "strawberry" variety, the cancerous gall-bladder; and such as show evidence of beginning, but definite, necrosis or impending gangrene. All such gall-bladders should very properly be removed. But too often, gall-bladders which do not fall within any of the above classes have been routinely resected on the grounds that the gall-bladder, from a surgical point of view, does not possess any necessary function, since certain patients do quite well without them. This point of view should be discouraged. For this group of gall-bladder cases, conservative surgery with postoperative medical drainage might be practised with wisdom. If non-surgical drainage methods are used, the "continuous" plan is the more practical method.

[1] Manges, W. F.: "*Non-surgical Drainage of the Gall Tract*" (Lyon), pp. 367–395.

[2] Graham, Cole: *Jour. Am. Med. Assn.*, 1924, **82**, 613; Graham, Cole, Copher, *Jour. Am. Med. Assn.*, 1925, **84**, 1175.

CHOLELITHIASIS[1]

Etiology.—Cholelithiasis is an exceedingly common condition, being found at autopsy in from 5 to 10 per cent. of subjects dead from all causes. It is specially prevalent in the temperate zones, being quite uncommon in the tropics. It occurs at all ages, but the incidence increases progressively with advancing years: 75 per cent. or more of the cases are found in persons over forty years of age, and less than 1 per cent. in those under twenty years; but this age incidence does not represent the time of the formation of gall-stones, since in many cases, having formed, they remain latent for years and are found when the subject dies at a more advanced age. Doubtless many gall-stones are formed in early adult life, before the fortieth year. Less frequently the disorder is encountered in infancy or childhood.[2] The majority of cases in infancy are doubtless due to intra-uterine infection, the process perhaps being analogous to that which in other circumstances induces congenital obliteration of the bile ducts; the cases in older children also may have originated during fetal life and remained latent for a number of years, but it is not always possible to exclude postnatal infections. Gall-stones are more common in women than in men, the ratio being variously stated as 5 to 1 (Schroeder) to 4 to 3 (Rolleston).

A most important factor is a low-grade inflammation of the biliary tract; a second requisite seems to be some obstruction to the free flow of bile. Other factors may possibly be in a defective function of the liver cells whereby, due to damage of some sort, they become unable to secrete a bile capable of holding in solution its normal crystalline substances, or the liver cells are incapable of handling an over supply of one crystal, such as cholesterin or calcium when a diet over-rich in cholesterol or calcium has been taken, or the liver cells are incapable of properly utilizing or metabolizing an increased amount of bile pigment in the various hemolytic diseases. The inflammation of the biliary tract is set up especially by typhoid and colon bacilli; but also apparently by attenuated streptococci, staphylococci, and other microörganisms that may cause acute cholecystitis; perhaps also by anaërobic bacteria. It was formerly thought essential that the antecedent catarrh be mild in grade, since in severe infections the mucosa of the gall-bladder is likely to be more or less destroyed and its cholesterin-producing function abolished. Recently

[1] The literature on cholelithiasis is so extensive as to make it inexpedient to give a reference list to individual articles, but the more important monographs comprise: Naunyn, *A Treatise on Cholelithiasis*, 1896; Kehr, *Gall-stone Disease*, 1901; Mayo Robson, *Diseases of the Gall-bladder and Bile Ducts*, 3rd edition, 1904; Moynihan, *Gall-stones and their Surgical Treatment*, 2d edition, 1905; Bland-Sutton, *Gall-stones and Diseases of the Bile Ducts*, 1910; Aschoff and Bacmeister, *Cholelithiasis*, 1909; Bacmeister, *Biliary Calculus*, 1913. Virtual monographs are contained also in Nothnagel's *Encyclopedia of Practical Medicine*, article by Hoppe-Seyler, and in Rolleston's *Diseases of the Liver, Gall-bladder and Bile Ducts* (literature). Valuable articles by Ewald, Musser, Brewer, Herter, Mayo and Kehr are contained in the *Tr. Cong. Am. Phys. and Surg.*, 1903, vol. **6**; and by Aschoff, *Lectures on Pathology* (Lecture 9, the *Origin of Gall-stones*), Hoeber, New York, 1924; by Naunyn (*Origin and Structure of Gall-stones*), *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1921, **33**, 2.

[2] Reid and Montgomery: *Bull. Johns Hopkins Hosp.*, 1920, **31**, 7; Farr, *Arch. Pediat.*, 1922, **39**, 574; Kellogg, *Ann. Surg.*, 1923, **77**, 587; Eusterman, *Ann. Clin. Med.*, 1924, **2**, 283; Fischer, A., *Jahrb. f. Kinderh.*, 1924, **104**, 350; Synder, *Jour. Am. Med. Assn.*, 1925, **85**, 31.

doubt has arisen as to whether the gall-bladder mucosa can produce cholesterin, or in any way help to manufacture it. The infective agents usually reach the gall-bladder by the portal circulation; variations in the source and pathways of infection are similar to those mentioned in acute cholecystitis. Kuru[1] studied by Weigert's fibrin stain sections of gall-stones and called attention to the importance of fibrin in their production.

Apart from infection of the biliary tract, a secondary requisite seems to be some obstruction to the free flow of bile. This occurs in circumstances similar to those mentioned in acute cholecystitis; but there are additional contributing factors. Thus gall-stones are especially common in those who lead a sedentary life, in women as contrasted with men, etc.; as part of the general muscular inactivity, the abdominal muscles and the diaphragm, contract relatively feebly and the bile, inefficiently expelled, stagnates in the gall-bladder.

In women a number of factors contribute. In addition to a more sedentary life, they are more often the subject of hepatoptosis or nephroptosis, that occasion more or less marked and continuous distention of the abdomen and interfere with the movements of the diaphragm. In consequence of the prolapse of the liver, the gall-bladder becomes dependent and the cystic or the common bile duct kinked, or perhaps has considerable traction brought to bear upon it and becomes obstructed, so that the gall-bladder is less easily emptied and is more disposed to infection. Tight lacing may act in a similar manner. The frequency of pelvic infections may be of some significance, either by serving as the source of the infection or leading to the formation of adhesions. The association of cholelithiasis with pregnancy is undeniable, but its importance is difficult to estimate, since the great majority of middle-aged women have been pregnant; there is some evidence, however, that gall-stones are more common in those who have been pregnant, especially repeatedly pregnant, than in those who were never pregnant. One very suggestive factor is that in the pregnant woman there is a well marked hypercholesterinemia, the cholesterin content of the blood increasing from the normal of 140 mg. per 100 cc. to 300 mg. or more. Perhaps in some cases puerperal infections are the cause of the gall-stones; sometimes the biliary infection can be definitely determined to have been acquired during the puerperium. Cholelithiasis is sometimes found with appendicitis; when the appendicitis precedes, the cholelithiasis and cholecystitis may have resulted from infection by the portal circulation; when the cholecystitis precedes, the appendicitis may perhaps result from the lodgment of infection in an unusually vulnerable organ.

Gall-stones show a relatively increased incidence in certain forms of heart disease, especially mitral and aortic valvular disease. This is doubtless due to several factors: the more sedentary mode of life incumbent upon chronic cardiac subjects, and the chronic congestive processes obstruct the flow and perhaps cause inspissation of the bile, reduce the resistance of the biliary tract, and favor infection. Similar factors account for the relative increase in the incidence of gall-stones in certain chronic pulmonary diseases.

[1] *Arch. f. path. Anat.* (etc.), Berl., 1912, **210**, 433.

Diet, disorders of the gastro-intestinal tract, and disorders of metabolism have long been credited with more or less etiological significance, but their exact influence is difficult to determine. Disorders of the gastro-intestinal tract associated with catarrh doubtless are of significance, since they may lead to extension of congestive processes to the biliary tract, provide bacteria that may induce catarrhal disorders in the bile ducts, and are a source of toxic products that exert a deleterious influence on the biliary passages. Dietetic and other indiscretions are of at least indirect influences in causing gall-stones; a vicious circle is formed in that cholelithiasis and the antecedent cholecystitis not only are frequently manifested by misinterpreted symptoms of so-called dyspepsia or indigestion, but lead directly to gastro-intestinal catarrh, and in virtue of the commonly associated pericholecystic adhesions induce more serious disturbances of the stomach and intestines. Constipation is probably of some etiological significance, largely by the attendant sluggishness of the intestinal circulation.

Whether diet as such is of real etiological significance is difficult to determine. It is believed that the gall-bladder empties physiologically in response to foods entering the duodenum. An important stimulus to gall-bladder contraction is the conversion of protein into proteoses and peptones when acted upon by acid gastric juice. Clinically the majority of cases of cholecystitis without stones have a normal, or high fractional gastric acid curve, whereas the majority of cases of calculus cholecystitis yield curves of lowered to absent acidity values. Habits of meal skipping are objectionable and frequent food taking in small quantities is desirable. Heavy eating and the excessive use of alcohol are doubtless of importance, especially by virtue of the gastro-intestinal catarrh and the chronic congestion of the portal system that they lead to; whether they are of additional significance, by virtue of disturbances of metabolism, is not definitely known, although it is widely believed in. Perhaps an excessive amount of food is of more significance than its character, although it is said that a carbohydrate or fatty diet disposes to, and a protein diet disposes against, the formation of gall-stones. Since it is now generally believed that the precipitation of cholesterin is due to catarrh of the biliary tract, the supposition that a carbohydrate diet leads to such precipitation by reducing the bile acids, the solvents of cholesterin, has lost much of its supposed importance. Naunyn's statement that even in diseased conditions the bile scarcely if ever contains so much cholesterin that it cannot take more in solution is questioned by some, since the bile from non-surgical drainage often shows enormous numbers of cholesterin crystals thrown out of solution in the bile. This has also been noted after a diet rich in cholesterol has been given, resulting in a hypercholesterinemia. Miyake[1] found gall-stones in but 3.05 per cent. of 8406 autopsies in Japan. The sexes were nearly equally affected. Japanese women do not wear corsets and Miyake believes this reduces the incidence in the female sex.

[1] *Archiv. f. klin. Chir.*, 1913, **101**, 54.

Pathology.—Gall-stones may be single or multiple; there may be one or thousands (7802 in a case of Otto's). In most cases the number varies between a dozen and a hundred; most of those in excess of a hundred are small and are spoken of as biliary sand or gravel. The stones vary much in size—from the smallest particle to those larger than a normal gall-bladder. Merkel found a gall-stones measuring 15 cm. in length and 12 cm. in circumference, Frerichs one that weighed 120 gm. and Ritter one that weighed 135 gm. When there are many stones, most of them are usually small; when there are few, there may be several rather large stones; when there is only one, it may be small, moderate in size, or very large, even completely filling, a distended gall-bladder. Gall-stones vary in shape. The large single stones, or several stones that fit together, conform to the shape of the interior of the gall-bladder, and are therefore ovoid or somewhat pear-shaped. Small single stones are usually ovoid or spheroidal. Multiple stones are usually cuboid or polyhedral, and exhibit variously shaped surfaces (facets), quadrangular, polygonal, etc., which being opposed to one another are usually smooth and polished, although it is doubtful if this results from mutual attrition; the edges of these stones are rounded rather than sharp. Stones within the intra-hepatic ducts conform to the ducts in shape, and are ovoid or cylindrical; occasionally they are branched, as are the ducts. Although usually smooth, the surface of gall-stones may be rough, irregular, or nodular (mulberry calculus; jack-stone calculus). In consistency gall-stones vary, depending upon the age and the chemical composition, the recently formed and the cholesterin stones being the softest; older stones may be hard and crumble readily, especially after being dried.

The following varieties of gall-stones are distinguished by Naunyn: (1) Pure cholesterin stones, which consist of nearly pure cholesterin and are uncommon. They vary in size from that of a cherry to that of a pigeon's egg, are hard, oval, or roughly spherical, seldom faceted, have a smooth or nodular surface, and are pure white or yellowish and translucent, or rarely brown, greenish, of brownish black on the surface. On section they are white and crystalline throughout, or show brown deposits between the crystals; they are not stratified. (2) Laminated cholesterin stones, which consist of about 90 per cent. of cholesterin, together with bilirubin calcium, biliverdin calcium, and calcium carbonate. In general appearance they resemble the pure cholesterin calculi, but they may be brittle and friable, and they are often faceted. On section they are more or less distinctly laminated, layers of almost pure white alternating with others that are yellow, brown, green, or red. The centre may be crystalline, but the external layers are usually vitreous or earthy. (3) The common (or mixed cholesterin) stones, which vary much in size, although they seldom equal a large cherry; they may be small and very numerous, and are usually faceted. The surface is usually yellow, but often brown or white. When fresh they are often soft and greasy; when dried they undergo shrinkage and become harder. On section the centre is often soft and may contain a cavity. (4) Mixed bilirubin-calcium stones, which may consist roughly of 75 per cent. of bilirubin calcium, and about 25 per cent. of cholesterin. They are as

large as a cherry or larger, and may occur singly or in groups of three or four in the gall-bladder or larger ducts. Their shape depends upon their situation; when multiple they may be faceted. They consist of concentric layers of reddish-brown or dark-brown material, which is seldom quite hard, and contracts on drying often with the formation of fissures or cracks. (5) Pure bilirubin-calcium stones, which vary in size from that of a grain of sand to that of a pea. There are two types: small, solid, brownish-black concretions, with rough irregular surfaces and wax-like consistency, and exhibiting a disposition to become welded; and harder, smooth concretions of a grayish-black metallic lustre and an internal spongy structure. (6) Rarer stones, such as amorphous and incompletely crystalline cholesterin gravel (resembling pearls); calcareous stones; concretions with included bodies and conglomerate stones; and casts of the bile ducts.

Gall-stones may be found in any part of the biliary tract. Of 216 patients operated upon for infections of the biliary tract by John B. Deaver, 182 (84.2 per cent.) had gall-stones. Of the 182 with gall-stones, 101 (55.5 per cent.) had stones in the gall-bladder alone; 23 (12.5 per cent.) had stones in the gall-bladder and cystic duct; 19 (10.5 per cent.) had stones in the gall-bladder and common duct; 12 (6.6 per cent.) had stones in the common duct alone; 11 (6 per cent.) had stones in the cystic duct alone; 5 (2.8 per cent.) had stones in the gall-bladder, cystic, hepatic, and common ducts; 4 (2.2 per cent.) had stones in the gall-bladder, cystic, and common ducts; 2 (1.1 per cent.) had stones in the adhesions (not otherwise specified); and 4 (2.2 per cent.) had stones in regions not definitely specified. Of the 216 patients, 58 had no stones in the gall-bladder, and of these, 23 had stones in the ducts; 41 had stones in the common duct, and of these, 12 had stones nowhere else; 9 had stones in the hepatic ducts (as well as elsewhere). Of 553 cases operated upon for gall-stones, Rovsing[1] found a single stone in 84 cases, multiple stones in 442 cases and gravel in 27. In 15.8 per cent. he found from 100 to 600 calculi, and up to 1000 and 4000. He comments on the fact that multiple calculi are as a rule nearly all of about the same size as if they had all been produced at one time and in the same manner. Rovsing reviews the various theories proposed to explain the production of gall-stones and presents data which oppose Naunyn's theory of the indispensable association of infection and stasis in the gall-bladder. In 530 of his cases studied bacteriologically, the bile was sterile in 60 per cent. Only in respect to typhoid infection was Naunyn's theory confirmed.

Pathogenesis.—In consequence of bacterial infection of the biliary tract a low-grade inflammation is set up; this, on the one hand leads to obstruction to the free flow of bile from swelling of the mucous membrane, and the products of this inflammation contain the essential constituents of gall-stones. In the gall-bladder the catarrhal inflammation leads to desquamation of the lining epithelium, an exudation, and an increased formation of mucus and, as some believe, of cholesterin; and in the gall-bladder dynamic factors frequently favor the stagnation of bile. The

[1] *Acta Chirurgica Scandinavica*, Stockholm, 1923, **56**, 103 and 206.

increased cholesterin is not wholly derived from the bile; it is said to result from catarrhal disintegration of the mucous cells lining the wall of the gall-bladder. The second important constituent of the gall-stones, bilirubin-calcium, is derived from the bile, being precipitated by bacterial growth or by the albuminous exudation of the inflammatory process—a phenomenon that can be imitated by adding egg-albumen to normal bile. It has been shown that bacteria, notably the typhoid and the colon bacillus (but not streptococci), may effect directly a decomposition of the bile with the precipitation of cholesterin. Exner and Heyrovsky attribute this to decomposition of the bile-acid salts (the solvent menstruum), in consequence of which the normal amount of cholesterin is no longer held in solution. Stagnation and inspissation of the bile do not give rise to the increased formation of cholesterin nor to the precipitation of bilirubin-calcium—whence they are contributing factors only. Bilirubin-calcium is believed by Naunyn to act as a cement substance, binding together the cholesterin, desquamated epithelium, etc., the whole forming the nucleus of the gall-stone. The exact significance of foreign bodies and of chemical substances apart from bacterial products has not been determined. There being no cholesterin-bearing mucous membrane in the smaller bile ducts, cholesterin gall-stones are not formed within the intrahepatic ducts, although by a retrograde movement they may be transported thither; bilirubin-calcium stones only are formed in the intrahepatic ducts; but both varieties are formed within the gall-bladder. Rous and McMasters[1] believe that the concentrating activity of the gall-bladder is a most potent element in the formation of stones; and that intermittent biliary stasis is the principal predisposing cause of cholelithiasis; and that such stasis is brought about through the excessive biliary inspissation made possible by the concentrating activity of the gall-bladder.

Associated Lesions.—Cholecystitis and cholangitis are common concomitants. The gall-stones may be free in the gall-bladder or the ducts, although usually more or less confined by the associated inflammatory processes; in some cases the stones may be adherent to the mucosa, especially in the gall-bladder; in other cases there is more or less incrustation of the wall, a deposition in the wall of cholesterin.

The consequences of gall-stone activity may be mechanical or inflammatory or both. The mechanical consequences follow what may be designated wandering of the stone into and through the biliary passages. Probably the most important and serious effects comprise permanent and complete obstruction of the common bile duct. Of only less importance are the dragging sensations and discomfort attendant upon the weight of many gall-stones in a distended gall-bladder; the gradual production of a Riedel or a linguiform lobe of the liver; the effects of pressure on adjacent organs; complete obstruction of the cystic duct, which, as a rule, leads at first to some distention of the gall-bladder, but soon to absorption of the bile and its replacement by mucus (hydrops) and gradual shrinkage of the gall-bladder, etc. These acquire their major importance from the opportunity that they afford for bacterial infection.

[1] *Jour. Exper. Med.*, 1921, **34**, 75.

This *infection* of the biliary tract is of the utmost significance, and forms an integral part of so-called calculous cholecystitis and cholangitis. The ensuing lesions are of the greatest diversity. The inflammatory phenomena may be of varying grades from the mildest catarrhal lesions to widespread phlegmonous and ulcerative processes; gall-stones, if present, may be quiescent or active; they may cause an acute or chronic partial or complete, temporary or permanent, obstruction of the cystic, the hepatic, or the common bile ducts, and, on the other hand, such obstruction may occur in the absence of gall-stones (swelling of the mucous membrane, kinking of the ducts, or obstruction from without), and in the presence of gall-stones the ducts may be partially or completely patulous. The gall-bladder may be distended or contracted, its walls thinned or much thickened, and its lumen ultimately may become almost if not quite obliterated; it may contain bile, mucus, blood, or pus, or combinations of these, in addition to or in the absence of gall-stones; adhesions may form between the gall-bladder and adjacent structures, and by way of the adhesions the gall-stones may rupture into the gastro-intestinal tract and sometimes cause intestinal obstruction; or purulent pericholecystitis and pericholangitis, localized or generalized peritonitis, pylephlebitis, pericholangitic abscesses of the liver, fistulæ, acute and chronic pancreatitis, etc., may ensue; and finally, in some cases, a general bacterial, often pyococcic infection, with or without multiple abscesses, may develop.

Symptoms.—The symptomatology of gall-stones is extremely variable, and one may perhaps speak of the immediate and the remote consequences, but in many cases differentiation is quite impossible. One may also speak of the mechanical and the infectious phenomena, the aseptic and the septic phenomena of the French writers; this in many respects is a serviceable classification, but the one set of phenomena by no means can always be differentiated from the other, and the one frequently follows the other or they occur together. The symptomatology is further complicated by the fact that in different cases the symptoms may be due to the gall-stones themselves, or to the associated infectious cholecystitis or cholangitis, pericholecystic adhesions, disease of related or adjacent organs, etc. One may, however, differentiate (1) a general symptomatology, and (2) certain special phenomena due to obstruction of the cystic or common duct, and (4) complications and sequels.

General Symptomatology.—The characteristic and significant symptoms are: (1) Chronic, long-continued, or recurring indigestion, called by Moynihan "inaugural symptoms," and (2) the phenomena designated gall-stone colic. The symptoms of chronic long-continued or recurring indigestion are of the utmost importance and are commonly misinterpreted. This stands in relationship with the facts that gall-stones are present in very many subjects and are commonly believed not to cause noteworthy symptoms; that symptoms, having once occurred, are exceedingly likely to recur; and that the symptoms are often paroxysmal and very severe.

It is widely believed that gall-stones are usually latent, and that only a very small percentage of gall-stone subjects (commonly estimated at 5 per cent.) manifest noteworthy symptoms. Gall-stones are sometimes

latent, particularly in elderly subjects in whom the original infection has died out, and in whom more or less atrophy, especially of the muscular coat of the gall-bladder and biliary ducts, has occurred; but it is now well known that the symptoms commonly denominated "stomach trouble," "indigestion," "dyspepsia," etc., are partly due in many cases to disease of the biliary tract. In a number of cases in which gall-stones are an accidental finding at the necropsy, investigation of the past history reveals many and often long-continued attacks of "indigestion;" the stomach is often found normal—in which event the gall-stones, cholecystitis, or pericholecystic adhesions serve to explain the clinical symptoms. Moynihan[1] thus describes his so-called "inaugural symptoms." "The patient complains of a fullness, weight and distention or oppression in the epigastrium coming on soon after meals, within half or three-quarters of an hour, relieved by belching and dismissed almost on the instant by vomiting, elicited with remarkable constancy by certain articles of diet, especially those of a 'greasy' nature and depending rather upon the quality than on the quantity of the food. There is a sensation of great tightness which if unrelieved may become acute pain from which the patient obtains ease by bending the body forward, by flexing the right thigh on the abdomen, or by loosening all garments which fit tightly to the waist. There is frequently great complaint of 'acidity' or heartburn, and in the act of belching there may be sour or acid regurgitation. While the discomfort lasts the patient may notice a 'catch' in his breath and he finds, perhaps, that it is impossible to breathe deeply without feeling an acute stabbing pain at the right costal margin. There may be a feeling of faintness and nausea, and, rarely, vomiting may occur spontaneously. After a more than usually severe attack of 'indigestion' the body and side may feel stiff for several days. A frequent and characteristic early symptom is the occurrence, during an attack of indigestion, of a slight sensation of chilliness, especially in the evenings after a meal. The sensation of 'goose-flesh' is often experienced."

Gall-stone colic usually develops suddenly with severe, often agonizing, pain in the right hypochondrium or the epigastrium, radiating around the chest or to the right scapular region; with nausea, vomiting, and prostration—weak pulse, rapid heart action, profuse perspiration, etc. Sometimes the attack is preceded by less acute, local pain or discomfort, chilliness, fever, etc.; more commonly (60 per cent. or more of the cases) chilliness and fever accompany and follow the pain. In some cases the severe pain lasts for a few moments only; usually it lasts for from two to twelve hours; in unusual cases it may last much longer, but in these circumstances the phenomena are more correctly interpreted as a succession of paroxysms. Often the pain ceases as suddenly as it began, but, usually following the agonizing pain, more or less dull aching continues for a variable period. The sudden cessation of the severe pain may be interpreted as a sudden relief of tension to which the gall-bladder has been subjected, due to opening of the cystic duct by the

[1] *Brit. Med. Jour.*, 1913, i, 8.

dropping of an obstructing gall-stone into the gall-bladder or the passage of the stone from the common duct into the intestine; in this event the calculus may subsequently be found in the stools.

In the great majority if not in all cases local examination reveals tenderness, abdominal rigidity, and the other local phenomena of acute cholecystitis. The colic may recur at varying intervals—days, weeks, months, or years; occasionally there is only one attack; usually there are many; with succeeding attacks the likelihood of other attacks increases.

The pains of cholelithiasis may be colicky or non-colicky. Although there is some discussion as to the cause of the colicky pain, there is little or no objection to attributing the non-colicky pain to inflammatory phenomena provoked by infection, inflammation of and about the gall-bladder and biliary ducts. The dull, aching pains are with excellent reason ascribed to inflammatory changes in the gall-bladder, with the exudation of inflammatory products and consequent distention. The more acute pains, associated with muscular rigidity, tenderness, etc., are due to infection of the regional peritoneum, which as it subsides occasions peritoneal adhesions, a contributing factor in the dull, aching pains, and of other significance. Some considerable distention of the gall-bladder is possible without provoking noteworthy pain, provided the cystic and the common ducts are patulous. It is to efficient drainage that the comparatively symptomless course of some cases of cholelithiasis is to be attributed, although the absence of inflammatory phenomena in the wall of the gall-bladder and the ducts, and the absence of adhesions, are also of significance. As regards the referred pains, although the sympathetic nerve is of significance, the demonstration that filaments of the pneumogastric nerve are distributed to the gall-bladder serves to explain the common association of gastric and cardiac symptoms with disease of the biliary tract; and the frequent occurrence of pain, sometimes of actual colic, three or four hours after a meal, suggests a causal relationship to the normal physiological contraction of the gall-bladder induced by the entrance of the chyme into the intestine.

As regards the colicky pains, there is no doubt that heretofore we have been too much concerned with interpreting them as evidence of the passage of a gall-stone through the biliary ducts; pains of like character may doubtless be due to different factors, which have been described by Riedel, who gives the following as the causes of gall-stone colic: (1) Adhesions of a gall-bladder no longer containing stones; (2) adhesions when large stones are present in the gall-bladder and the cystic duct is patent: (3) inflammatory processes in a gall-bladder distended by fluid or stones, when the cystic duct is occluded by inflammation or by the presence of a stone in the neck of the gall-bladder; (4) the transit of a stone through the bile passages; and (5) the inflammation of a dilated common duct or its tributaries without impaction of the stone.

There can be little doubt that in a number of cases the spasmodic efforts of the gall-bladder and the common duct to expel their contents by vigorous contraction of their muscular coats are the cause of the peculiar gall-stone colic. This pain occurs in its greatest intensity during

the transit of a stone through the ducts, and it ceases as the stone is discharged into the intestine or drops back into the gall-bladder—thus freeing the cystic duct. But there also can be little doubt that attacks of pain indistinguishable from those provoked by the transit of a stone may be due to other factors—those mentioned above; although in some instances the attacks of pain may not be so severe as those of a so-called true gall-stone colic. If the obstruction be incomplete, hypertrophy of the muscular coat results, and later often lessening of the size of the cavity; whereas, if the obstruction be complete, paresis of the muscular coat soon occurs, dilatation ensues, and the pain subsides. But, as exemplified by the 216 patients already mentioned, gall-stones are absent in 15.5 per cent. of the patients who have colicky pains, and they are present in 77.7 per cent. of the patients who have only non-colicky pains. There is a type of colic clinically inseparable from gall-stone colic, which has sent patients to the operating table but in whom at operation, no stones were found in the gall-bladder or in the ducts. Nor was there any evidence to suggest that a stone had been passed. The writer believes that the mechanism by which this colicky pain is produced may be attributed to simultaneous spasm or contractural effort of an inflamed gall-bladder acting against a tonically contracted sphincter of Oddi, producing a rise of intraduct or intracystic tension upon inflamed mucous membranes; or to irregular spasmodic contractural efforts on the part of an inflamed gall-bladder acting against a cystic duct obstruction. He believes that either condition may exist as an entity and closely simulate gall-stone colic.

Cases of protracted colic may be looked upon as due to long-sustained efforts of the gall-bladder to overcome the obstruction to the egress of its contents, or to slow progress of a calculus along the ducts, the consequence of the large size of the stone or the spiral arrangement of the Heisterian valve which retards progress. Gall-stone colic, therefore, although it is often due to the passage of a gall-stone along the ducts, should be interpreted rather as evidence of acute cholecystitis (or acute exacerbation of chronic cholecystitis): an interpretation sustained by the concomitant occurrence of enlargement and tenderness of the gall-bladder, fever, chilliness, leukocytosis, etc.—the ordinary signs of acute cholecystitis. Furthermore, as the inflammation subsides the stones become quiescent and the symptoms subside.

Jaundice is a common but not a necessary feature and may come on a variable time after the pain—a few hours or several days; that is, when the obstruction has reached the common duct. It varies in degree and duration with the local conditions. If the obstruction results from the traumatism and consequent catarrh due to the passage of a stone it may be moderate and pass off within a week or thereabouts—as the swelling subsides and the duct becomes again patulous. Should the obstruction be more complete and the stone not be discharged, the jaundice may become quite extreme and lasting; but a large stone may be in the common duct without causing jaundice.

The jaundice of cholelithiasis is mechanical or obstructive and may be due to (1) gall-stones in the hepatic or the common bile duct; (2)

spasm of the musculature or inflammatory swelling of the mucosa of the biliary ducts; and (3) compression of the common duct or of the extrahepatic part of the hepatic duct by a large stone in the cystic duct, swollen lymph glands, regional tumors, inflammatory exudations, adhesions, kinking of the ducts, etc. The practical deductions to be drawn from the known facts are: (1) That in some cases of cholelithiasis jaundice is not due to obstruction of the ducts by a stone but rather to infection, inflammatory swelling of the ducts, and (2) that in many cases of cholelithiasis jaundice does not occur at all, although other important and distressing symptoms may be quite obtrusive. Of 216 patients, 74 (34.2 per cent.) never had jaundice; 141 (65.3 per cent.) had no jaundice at the time of operation; whereas 121 (56 per cent.) gave a history of attacks of jaundice prior to the time of operation. These attacks, in some cases, antedated the operation many years; in some cases long periods of freedom from jaundice followed; in some cases there were no subsequent attacks of jaundice. Moynihan finds that 25 per cent. of the patients from whose common ducts stones are removed have never been jaundiced.

The *gall-bladder* may or may not be enlarged and palpable. Thus, of 216 patients, in 88 (40.7 per cent.) the gall-bladder was enlarged; in 9 (4.1 per cent.) the gall-bladder was normal in size; in 32 (15 per cent.) the gall-bladder was small and atrophic; and in 87 (40.2 per cent.) the size of the gall-bladder is not known.

Special consideration has been given to the diagnostic importance of the size of the gall-bladder. Courvoisier, basing his opinion upon an analysis of 187 cases, stated that in cases of chronic jaundice contraction of the gall-bladder is suggestive of gall-stones, and that dilatation of the gall-bladder is suggestive of biliary obstruction caused by factors other than gall-stones—that is, pressure from without, most often carcinoma of the head of the pancreas. This law serves well in the majority of cases, although as Courvoisier admitted there are notable exceptions. In at least 40.5 per cent. of 116 patients who had gall-stones and jaundice the gall-bladder was enlarged. In somewhat more than one-half of these cases, however, gall-stones were present in the gall-bladder alone, and the associated jaundice was doubtless due to inflammatory swelling, pressure from without, etc. Courvoisier's explanation of the shrinkage of the gall-bladder in these cases is correct; that is, it is due to inflammatory thickening and cicatrization, the consequence of repeated infection. This process requires time—whence the condition of the gall-bladder varies early and late in the disease. That such cicatrization does occur is suggested by its presence in a number of cases in which gall-stones were present without jaundice. It is impossible that a thickened and cicatrized gall-bladder should dilate, no matter what the obstruction in the common duct. One can conceive, however, of an acute cholecystitis or empyema of the gall-bladder (with distention) and an acute impaction of a stone in the common duct (with jaundice); or of hydrops or empyema of the gall-bladder (with distention) and a large stones in the cystic duct compressing the common duct (with jaundice); or the association of a stone in the common duct and carcinoma of the head of the pancreas, in which event the gall-bladder might be dilated, or small, thickened, and atrophic or sclerosed.

Sometimes when the gall-bladder contains several stones and its walls are not too tense, gall-stone *crepitus* may be elicited by palpation. This is valuable diagnostically when the symptoms are not frank.

As already stated, *fever* is common in cholelithiasis. Of 216 patients, 143 (66.2 per cent.) had fever some time during the course of the disease; 65 (30.1 per cent.) had no fever while under observation; and in 8 (3.7 per cent.) there is no note of the presence or absence of fever. This fever is a manifestation of infection, and is not due merely to reflex causes, nervous perturbations, etc., as was at one time though. In many cases, concurrently with the development of the gall-stone colic, there is a sudden elevation of the temperature, followed sometimes by an equally sudden fall; the onset of this fever may or may not be associated with chilliness or a definite chill; in other cases the fever is of somewhat longer duration, and is due to an acute cholecystitis or an acute exacerbation of chronic cholecystitis; in other cases the fever is slight and perhaps it is sometimes absent—evidently cases of chronic low-grade infection; in other cases, especially cases of calculus in the common bile duct, the fever is that known as Charcot's intermittent hepatic fever—periodic attacks of chill, fever (102° to 104° F.), and sweats, accompanied by pain, recurrence or increase of jaundice, and perhaps nausea and vomiting.

Obstruction of the Cystic Duct.—The calculus is usually lodged in the beginning of the duct or in the termination of the neck of the gall-bladder. The following conditions may ensue: (1) Acute cholecystitis (catarrhal, suppurative, phlegmonous, or gangrenous). (2) Chronic dilatation of the gall-bladder, a condition that follows complete obstruction to the entrance of bile into the gall-bladder, which soon becomes distended with mucus, at first bile-stained, but ultimately quite clear. The gall-bladder content is perhaps partly inflammatory, in the beginning at least, but in many cases the infection gradually subsides, whereas in others it becomes relighted or a new infection and acute cholecystitis ensue. (3) Chronic fibrous or atrophic cholecystitis—the usual sequel of hydrops when the obstruction is not complete and the infection dies out. The gall-bladder gradually becomes reduced in size and may ultimately be reduced to a mass of fibrous tissue, which usually tightly encircles a calculus. When the gall-bladder becomes small and contracted, symptoms may be in abeyance, or they may be those of chronic cholecystitis with or without acute exacerbations, or those of adhesions. Often there is incrustation of the wall with cholesterin; there may be diverticula which usually contain calculi.

Obstruction of the Common Bile Duct.—There may be one or many obstructing calculi; in the majority of cases there is only one, and this is usually in the lower end of the common duct or the diverticulum of Vater, but it may be in any part of the duct; when there are many calculi they may extend throughout the common duct into the hepatic duct and its branches and into the cystic duct and the gall-bladder. The obstruction may be complete or incomplete, and may or may not be associated with cholangitis. When the obstruction is complete a stone is usually tightly impacted in the common duct; when the obstruction is incomplete the stone may be more or less fixed, but permits the flow

of bile around it, or it may circulate in the common duct and imitate the conditions in a ball valve. A calculus originally tightly impacted in the common duct often, in the course of time, becomes more or less free, in consequence of atrophy or ulceration of the wall of the duct about the stone, or of dilatation of the duct above the stone. Dilatation of the ducts is a common event; it is usually cylindrical, the common duct not infrequently becoming as large or larger than one's finger; occasionally the dilatation is saccular, the common duct attaining the size of an orange; small saccular dilatations may also occur on the surface of the liver, especially the left lobe. The liver at first is usually somewhat enlarged from accumulation of bile; later atrophy of the hepatic cells ensues, and in consequence of biliary infection, inflammatory phenomena spread from the bile ducts to the adjacent tissue—cholangitis and pericholangitis. This gives rise to some new connective tissue, and the atrophy of the hepatic parenchyma causes a relative increase in the preëxisting connective tissue, so that a condition resembling cirrhosis is induced; but although a form of chronic hepatitis, this is not cirrhosis and it is at best doubtful if biliary stasis can lead to true cirrhosis.

The *clinical* manifestations of a stone in the common duct vary, depending whether the obstruction is complete or incomplete and whether or not it is associated with infection of the ducts. In the event of complete obstruction without infection, permanent and lasting jaundice is produced, unattended by fever and other signs of local infection. In the event of incomplete obstruction suggestive symptoms are sometimes absent, as a large stone may be present for years without jaundice. Usually, jaundice is present; it lasts a long time, and, varying with the degree of biliary obstruction, is subject to more or less fluctuation, which is very characteristic; and there is fever, periodic, intermittent, remittent, or more or less continuous, indicative of the concomitant biliary infection. This biliary infection is present in practically all cases of incomplete obstruction; it may continue for years without the advent of suppuration, but suppurative cholangitis and cholecystitis may ensue.

Naunyn gives the following as the characteristic signs of a calculus in the common bile duct: "The continuous or occasional presence of bile in the feces; distinct variations in the intensity of the jaundice; normal size or only slight enlargement of the liver; absence of distention of the gall-bladder; enlargement of the spleen; absence of ascites; presence of febrile disturbances, and duration of the jaundice for more than a year." Osler has emphasized the importance of the following signs in the diagnosis of a ball-valve calculus in the diverticulum of Vater (where it occurs most frequently), or in the common bile duct: "(*a*) Ague-like paroxysms of chill, fever, and sweating—the hepatic intermittent fever of Charcot; (*b*) jaundice of varying intensity, which persists for months or even years, and deepens after each paroxysm; and (*c*) at the time of the paroxysm, pain in the region of the liver with gastric disturbance. . . . Pain, which is sometimes severe and colicky, does not always occur. There may be vomiting and nausea. As a rule, there is no progressive deterioration of health. In the intervals between the attacks the temperature is normal."

When the calculus is situated in the diverticulum of Vater it may obstruct the duct of Wirsung, and should the duct of Santorini be unable, on account of non-communication, to divert the pancreatic juice into the duodenum, accumulation of the juice and dilatation of the ducts ensue; furthermore, the common infection present in these cases gradually spreads to the pancreatic ducts, producing *pancreatitis*, with early enlargement of the organ, especially the head, which may become so hard as to suggest carcinoma; later the organ becomes contracted and fibrosed; in some cases pancreatic lithiasis also ensues. Mayo[1] states that in 2200 operations upon the gall-bladder and biliary ducts the pancreas was found coincidently affected 141 times (6.1 per cent.); since the total number of operations undertaken for disease of the pancreas was only 168, it was found that 81 per cent. of the cases were due to or accompanied by gall-stones. In 268 operations upon the common and the hepatic ducts the pancreas was found diseased in 18.6 per cent., as contrasted with 4.45 per cent. of the cases in which the gall-bladder only was diseased.[2] In the event of incomplete obstruction of the pancreatic duct, bile may be diverted into it, and lead to the production of acute hemorrhagic pancreatitis.

Complications and Sequelæ.—Of the many complications and sequelæ of cholelithiasis, some infectious, some purely mechanical, but most of them infectious and mechanical, the following are the most important: (1) Infectious (inflammatory) lesions of the biliary tract and adjacent viscera; (2) chronic pericholecystic adhesions; (3) biliary fistulæ; and (4) intestinal obstruction.

Infectious (Inflammatory) Lesions of the Biliary Tract and Adjacent Viscera.—Having been formed, gall-stones participate in a vicious circle and keep alive the infective inflammation to which they owe their origin, so that inflammatory lesions of the biliary tract and adjacent viscera ensue. These comprise especially varying grades of acute and chronic, suppurative and non-suppurative, cholangitis and cholecystitis, progressing perhaps to ulceration, gangrene, perforation, etc. The inflammatory phenomena may extend to adjacent structures and set up peritonitis, pylephlebitis, pancreatitis, etc., or, in consequence of adhesions, they may seriously disturb the gastro-intestinal tract; or progressing to necrosis and suppuration they may lead eventually to the formation of fistulæ.

Chronic Pericholecystic Adhesions.—Adhesions are frequently encountered in the upper abdomen; of 216 patients, 123 (56.6 per cent.) had adhesions about the gall-bladder; 22 (10.1 per cent.) had no adhesions; and of 71 (33 per cent.) there is no note of the presence or absence of adhesions (probably none were present). These adhesions represent the sequels of past subacute and chronic, sometimes acute, inflammation of the organs of the upper abdomen, of which the biliary tract is the chief; whence they are a direct result of biliary infection.

The conditions are quite analogous to those in and about the vermiform appendix. Should the biliary infection be acute and virulent, a fibrinous

[1] *Jour. Am. Med. Assn.*, 1908, **50**, 1161.

[2] Mayo Robson: *Surg., Gynec., and Obst.*, 1908, **6**, 29; and Maugeret, *Cholecysto-pancréatite*, Paris, 1908.

exudation results. In the subacute and chronic infections, however, the formation of adhesions goes on less obtrusively, often entirely latently, whence the later symptoms are commonly misinterpreted. With milder infections the inflammatory phenomena are less sufficient, however, often to lead to more or less widespread adhesions. All gradations are encountered; quite localized and very delicate, resembling spider-webs, as aptly described by Morris; in other cases widespread and very dense.

The clinical recognition of these adhesions is sometimes a matter of difficulty, but it is perhaps not impossible in the majority of cases. It is essential, in the first place, that we recognize that many of the cases of so-called "stomach-ache," "biliousness," "indigestion," etc., in reality have an anatomical basis. Many of these cases are due to a gastric or duodenal ulcer, cholecystitis, chronic pancreatitis, etc.; in other cases they are due to adhesions. We must study attentively patients who complain of general ill health, with more or less ill-defined gastric or epigastric symptoms. Attacks of such symptoms may come on without definite cause; they may last a few days, and cease as causelessly. The attack may be ushered in with chilliness (rarely a definite chill), and be attended by a little fever. Examination may reveal some tenderness in the epigastrium, perhaps a little to the right of the median line, and some rigidity of the overlying muscle. Deep pressure is sometimes very painful. Later, should the pylorus or the duodenum become obstructed, the manifestations of dilatation of the stomach supervene. Special diagnostic importance attaches to intractability of the symptoms and a history of past infection of the biliary tract. In the event of suspecting such adhesions we must exclude other factors that may cause similar symptoms, remembering that in many cases symptoms supposedly due to disease of the stomach or intestine are due to disease of the gall-bladder or adhesions of the upper abdomen. Much has been accomplished in the study of these adhesions by means of the roentgen-ray. The use of the "tuning fork test" for adhesions has also proved of value.[1]

Biliary Fistulæ.—Fistulous communications between the biliary tract and adjacent viscera as well as the exterior of the body may result. Courvoisier in a study of 499 cases found that fistulous communications had been established between different parts of the biliary passages in 8; into the portal vein in 5; into the peritoneal cavity in 70; into peritoneal adhesion in 49; into the retroperitoneum in 3; with the stomach in 13; with the duodenum in 83; with the jejunum in 1; with the ileum in 1; with the colon in 39; with the urinary tract in 7; with the pleura and lung in 24; and externally in 196. The external fistulæ appear to be disproportionately numerous since they command attention, whereas the internal fistulæ frequently are not detected. In external fistulæ the opening may be near the normal situation of the gall-bladder, near the umbilicus (being directed thither by the falciform ligament), in the right iliac fossa, in the thigh, etc. Biliary, gastric and intestinal fistulæ are often unsuspected; sometimes they are first revealed by the discharge of gall-stones with the feces or by the sudden disappearance of long-standing

[1] Lyon: *Surg., Gynec., Obst.*, 1922, **35**, 232, and Ellison, *Arch. Int. Med.*, 1924, **34**, 721.

obstructive jaundice, or by the onset of intestinal obstruction. Broncho-biliary fistulæ lead to cough, dyspnœa, and the expectoration of pus, bile, and perhaps gall-stones.

Intestinal Obstruction.—This is a rather rare event that may follow ulceration of a gall-stone from the gall-bladder into the duodenum or, less commonly, the colon. It is doubtful if a gall-stone that has been able to pass through the ducts and the ampulla of Vater into the duodenum is large enough to obstruct the intestine; in some cases a comparatively small stone may be arrested at the ileocecal valve; it may set up inflammation and localized spasm of the intestine with consequent obstruction; it may become increased in size after it reaches the intestine (enterolith); or it may become arrested in a part of the intestine narrowed by disease. The ratio of gall-stone to other forms of intestinal obstruction varies between 1 to 13 (Fitz) and 1 to 45 (Barnard). Lesk[1] collected 148 cases, of which 109 (73.5 per cent.) occurred in women and 39 (26.5 per cent.) in men. Only 6 of the patients were less than forty years of age; most of them were beyond fifty. In 104 of Lesks' cases the obstruction was in the ileum in 62 (59.6 per cent.), in the jejunum in 17 (16.3 per cent.), in the small intestine (without definite statement) in 13 (12.5 per cent.), in the colon in 6 (5.7 per cent.), in the duodenum in 5 (4.8 per cent.), and in the rectum in 1 (1 per cent.). In 26 of the 62 cases in which the obstruction was in the ileum it was near the ileocecal valve. The diagnosis rests upon the advanced age of the patient and a past history of gall-stones or other manifestations of biliary infection; in some cases the gall-stones causing the obstruction and the adjacent tissues form a palpable mass in which the gall-stone may be distinguishable. In most cases, however, the cause of the intestinal obstruction cannot be diagnosed with certainty until it is seen. Sometimes the obstruction is relieved spontaneously, but at least one-half of the patients die unless relieved by surgical procedures. The operative mortality is high (about 45 per cent.), due largely to delay, but also to the advanced age of the subjects.

Diagnosis.—This comprises the recognition of the gall-stone colic and of the many and varied associated lesions and sequels. Severe pain in the epigastrium or the right hypochondrium, radiating around the chest or to the right scapula, accompanied by nausea and vomiting and enlargement and tenderness of the gall-bladder, and followed by jaundice and the detection of a gall-stone in the feces, are characteristic of the passage of a gall-stone; but jaundice is by no means always present and the other symptoms may be provoked by cholecystitis in the absence of a gall-stone; indeed, with increasing experience it becomes often more and more difficult to say whether or not gall-stones are present in certain cases of obvious chronic biliary infections.

Recourse to roentgen-rays is of great aid since in approximately 50 per cent. of cases positive gall-stone shadows can be demonstrated by proper technique (Manges).

The finding of large masses of cholesterin plates or of calcium or bilirubin crystals in the biliary drainage sediments of patients complaining

[1] *Deutsche Ztschr. f. Chir.*, Leipz., 1908, **99**, 47. Also Gutiérrez, *Rev. de Cirugia*, Buenos Aires, 1924, **3**, 45.

(or not complaining) of gall-stone types of "indigestion" is presumptive evidence that they have gall-stones, either formed or in process of forming. The recovery, by drainage, of gall-sand makes the diagnosis certain.

A diagnosis after the event is readily made in many cases, but during the severe pain one may be unable to determine the cause. A few whiffs of chloroform or a hypodermic injection of morphine may so relieve the patient as to permit of an examination, in which event tenderness and perhaps enlargement of the gall-bladder may be found. The severe pain of gall-stone colic may be imitated by renal or intestinal colic; but in renal colic the pain is usually in the back, loin, or groin, and radiates down the ureter to the testicle, which may become retracted; strangury or frequent micturition is common; the kidney is usually tender (the tenderness being in the loin rather than anteriorly; and the urine subsequently contains blood and a proportionate amount of albumin, perhaps crystals or a calculus, and pus and epithelium from the pelvis of the kidney; and it does not contain bile. Intestinal colic is usually due to some more or less obvious cause; the pain is usually about the umbilicus, it radiates in different directions, remits and intermits, and subsides with the removal of the exciting cause, often with belching or the discharge of feces or gas or mucus by the bowel; and there is no localized tenderness in the region of the gall-bladder. In lead colic there is the history of exposure to the poison, a blue line on the gums, anemia, basophilic degeneration of the erythrocytes, etc.

When the symptoms, especially the pain, are less acute, and do not merit the designation gall-stone colic, difficulty may be experienced in differentiating disorders of the stomach. Much assistance will be obtained by bearing in mind that the patient with "chronic indigestion" who is not benefited by well-directed therapy commonly has an anatomical cause. Gastric or duodenal ulcer is suggested by dependence of pain upon taking food or its occurrence as the chyme passes into the duodenum (which sometimes obtains also in cholelithiasis), by tenderness in the median line or slightly to the right, and posteriorly on the left side near the vertebræ, hyperchlorhydria, hematemesis, etc., and the absence of jaundice and fever; prominence of nausea and vomiting is more significant of cholelithiasis. Pericholecystitis and perigastric adhesions are often the cause of chronic indigestion, and may cause pyloric obstruction and gastric dilatation.

Malignant disease of the gall-bladder usually follows cholelithiasis, but so insidious, as a rule, is its onset that it is commonly not suspected until the loss of flesh and strength and the progressive development of cachexia. In some cases of more or less apparent cholelithiasis the diagnosis of carcinoma is favored by the detection of progressive nodular enlargement of the gall-bladder, and in some cases by the occurrence of metastasis to the liver, ascites, etc. In the event of jaundice, its persistence unchanged suggests malignant disease of the ducts or pancreas, etc., although it may be due to a stone tightly impacted in the common duct; but there is less impairment of the general health than in carcinoma; in the majority of cases of gall-stones in the ducts, as contrasted with malignant disease or catarrhal cholangitis, there is periodic variation in the intensity of the jaundice and fever (intermittent hepatic fever).

Prognosis.—The prognosis, as a rule, depends more upon the associated conditions than upon the mere presence of the gall-stones. The prognosis in gall-stone colic is virtually that of a more or less acute cholecystitis; the outlook as regards permanent health depends upon the chronic gall-bladder infection. In almost all cases of gall-stone colic the acute symptoms subside spontaneously after several hours or several days; rarely a patient may die, it is said, from shock and cardiac failure; occasionally rupture of the gall-bladder ensues and give rise to infectious peritonitis and a fatal issue; and in other cases a stone impacted in the neck of the gall-bladder or the cystic duct and the attendant infection and interference with the blood supply may, after the lapse of several days, lead to severe suppurative or gangrenous cholecystitis.

A first gall-stone colic is sometimes the last and the infection subsides. Usually, however, there are subsequent attacks, if not of severe colic, of more or less disturbance with digestion, and general impairment of health, due to the toxic absorption, etc.; some subjects pass into chronic invalidism. The likelihood of continuation of symptoms is increased by the duration of symptoms in the past; that is, those already ill for some time are likely to continue ill, and the lesions to progress. The detection of faceted stones in the feces suggests that other stones are still undischarged; the detection of rounded or ovoid stones in the feces, together with subsidence of the local symptoms, arouses the hope that there was but a single stone. The occurrence of intermittent hepatic fever, especially of severe paroxysms, renders the prognosis rather bad, since it shows active infection, which, although it may persist for years without suppuration, may lead to serious consequences. The prognosis as to final recovery of health is bad in pericholecystic adhesions, fistulæ, and intestinal obstruction without operative intervention.

Treatment.—The intelligent treatment of cholelithiasis presupposes a clear conception of (1) the pathology, the pathogenesis, pathological anatomy, and natural tendencies, and (2) of the means of treatment and the objects attainable. To attempt by internal medication to dissolve a gall-stone that is insoluble; to cause the passage through the biliary ducts of a gall-stone when the ducts are impassable to a stone of its size; to attempt to cure supposed gastric symptoms by measures directed to the stomach when the cause is adhesions and to attempt the solution of these adhesions—is as futile as it is irrational.

Prophylaxis.—A knowledge of the etiology suggests certain measures of prophylaxis. Although we may be quite unable to prevent the causative infection in the individual, we may advise useful measures. The fact that gall-stones are most common in women, in the obese, in those who lead a sedentary life, eat too much, are constipated, and addicted to alcohol, suggests the correction of certain factors. Women who have been repeatedly pregnant and have lax abdominal walls should wear proper supports; and all women should avoid tight lacing. Men and women who lead a sedentary life should take proper exercise; they should practise deep breathing (to promote the movements of the diaphragm), bathe frequently, be much in the open air, etc. Constipation should be overcome, and the diet should be such as will be pointed out. If these

measures do not prevent the formation of gall-stones in those who have or have had a biliary infection, they will at least tend to reduce biliary infection, and perhaps obviate some consequences of cholelithiasis.

When gall-stones have formed, the main indications for treatment are: (1) To cause solution of the stone or stones; (2) to cause the discharge of the stone or stones; and (3) to treat the complicating infection.

Solution of the Gall-stones.—Naunyn[1] states that we have to consider cholesterin, bilirubin-calcium, calcium carbonate, and calcium phosphate. Bilirubin-calcium and the inorganic salts of calcium are insoluble in the bile; cholesterin is quite soluble in the bile, and even in conditions of disease the bile scarcely if ever contains so much cholesterin that it cannot take more in solution. We have, therefore, to admit the possibility of cholesterin stones being dissolved. There is some experimental evidence that not only *in vitro*, but also *in vivo*, cholesterin stones may be dissolved. Naunyn quotes Labes' experiments in which he introduced gall-stones into the gall-bladder of dogs, and, killing the animals two months later, found that partial solution of the stones had occurred. Bain[2] and von Hansemann[3] have published the results of studies that show the same possibility. In these experiments, however, the calculi were introduced into normal gall-bladders (or, as in some of Bain's experiments, into gall-bladders in which a cholecystitis has been artificially produced). The conditions are quite different in the human subject with gall-stones and it is exceedingly doubtful whether spontaneous solution of gall-stones ever occurs in the human subject—indeed, whether it is at all possible.

Judging from clinical experience, it is exceedingly doubtful whether, with any means at our command, we can cause solution of gall-stones in the gall-bladder. The thousands of gall-stones said to have been passed by the bowel after the administration of olive oil are masses resembling gall-stones (saponified oleic acid). There is no reason to believe that olive oil, derivatives of olive oil and other oils, turpentine, ether, etc., have any influence in dissolving gall-stones in the biliary tract.

Discharge of the Gall-stones.—This should not be hoped for nor awaited or sought by medical means, even were such at our command; it cannot be considered an object of rational treatment.

Treatment of the Biliary Infection.—The one worthy object is to restore the latency from which the gall-stones have been awakened—in other words, to control the infection at the basis of gall-stone activity. This must also be the object of treatment of cholecystitis in the absence of gall-stones. The infection and bile stasis of the biliary tract have to be treated. Non-surgical drainage of the biliary tract is the best weapon. The surgeon may remove the stones and also treat the biliary infection. The physician in many cases may lead his patient into a condition of virtual cure, that is, latency or sterility of the biliary tract; but he must recognize his limitations, and not subject his patient too long to useless treatment when early surgical intervention may restore him to health.

[1] *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, Jena, 1905, **14**, 53.
[2] *Brit. Med. Jour.*, 1905, ii, 269.
[3] *Arch. f. path. Anat.* (etc.), Berl., 1913, **212**, 1.

The *pain of gall-stone colic* is usually so severe as to require the administration of morphine, which not only relieves the pain (and mitigates the attendant shock) but, by relaxing the spasm of the biliary musculature, favors the exit of bile from the tense gall-bladder and the transit of the calculus through the ducts (if it be already therein). A few whiffs of chloroform or ether will usually carry the patient through the painful period until the morphine has time to act; or, and this is often attended with excellent results, an additional dose of atropine ($\frac{1}{100}$ gr.) may be administered hypodermically.

The use of coal-tar products for the relief of the pain is ill advised, since not only are they comparatively inefficacious but they also add to the depression of an already depressed patient; the salicylates and olive oil (even when tolerated) also are of no value during the acute stage, although olive oil by inducing vomiting may assist in dislodging the stone. Sometimes it may relieve an assocated hyperchlorhydria.

In many cases relief may also be afforded by hot fomentations over the region of the gall-bladder and by lavage of the stomach with water as hot as can well be borne; or by biliary drainage, although it is better to have recourse to the latter after the acute attack of pain has partially subsided. All food should be withheld during the continuance of the acute symptoms. Vomiting ceases with the cessation of the pain, so that the best treatment for the vomiting is that which tends to relieve the pain. Should the vomiting persist and be manifest especially by ineffectual retching, resort should be had to lavage: if it has not been previously used, sodium bicarbonate may be added to the hot water. A hot bath may be given at the beginning of the attack, with hope of excellent result. In other cases the vomiting may be relieved by gastric sedatives. In some cases the pain leads to extraordinary depression which, if not relieved by morphine, should be treated by the hypodermic use of camphor.

Upon the subsidence of the pain, as well as in the absence of a definite gall-stone colic, the medical treatment is that of the chronic biliary infection. By promoting the flow of bile one may effect the discharge of infecting bacteria and their toxins from the biliary passages and prevent their ascent to the smaller ducts, and by the constant irrigation one may allay the inflammatory phenomena. To this end, no single non-operative measure is of greater value than drainage of the biliary tract by duodenal tube, coupled, if possible, with the use of an autogenous vaccine. Ultimately, the biliary tract may be rendered sterile, and should the inflammatory phenomena subside completely a condition of latency of the gall-stones results. In rare cases this is permanent, and the patient experiences no further trouble. In most cases a low-grade chronic inflammation of the gall-bladder persists; in other cases the gall-bladder readily again becomes infected, and the patient is continuously or intermittently ill. Should gall-stones be passed by the bowel, one must remember that all the gall-stones are seldom, if ever, thus passed, and that even were this the case, the persisting inflammation is quite certain to give rise to the formation of new stones.

The *diet* should be carefully regulated and the intervals between meals should be such as tend to frequent and free emptying of the gall-

bladder. Cholelithitic subjects should have a sufficient but not an excessive diet; in character it should be based less upon the mere presence of gall-stones than upon the attendant gastro-intestinal catarrh, constipation, and jaundice (if present). In general a mixed diet is the best; this should contain considerable and varied protein, which is believed to promote an abundant supply of bile acids and to stimulate the flow of the bile. In the presence of jaundice, proteins and readily digested carbohydrates should be advised, and the fats should be much reduced or excluded for a time, since they are ill digested in the absence of bile; in the absence of jaundice it is theoretically unnecessary to prohibit fat on the mistaken apprehension that a fatty diet tends to increase the cholesterin in the bile. From a practical standpoint most patients with gall-stones or chronic cholecystitis, with or without adhesions, find that fats, eggs, and meats disagree. Therefore a diet in which the fats (butter, cream, ice cream, olive oil and all greasy foods such as bacon) and animal protein (eggs and meats except chicken or fish) have been reduced 50 per cent. or more will be best tolerated. Naunyn said that a full meal is an excellent cholagogue, so that with the hope of preventing stagnation of the bile an additional small meal may be given at bedtime, unless contraindicated. In most cases it is wise to prohibit the use of alcohol.

The utility of large amounts of water, especially of alkaline mineral waters containing sodium salts, is unquestionable. Since they have no solvent action on the gall-stones their beneficial effect is probably on the associated biliary and gastro-intestinal catarrh. There is some experimental evidence that these waters do not directly stimulate the flow of bile, and that the excessive amount of fluid does not dilute the bile, but this doubtless results indirectly, the removal of biliary constituents from the intestine leading to renewed formation; and an insufficient supply of water tends to inspissation and stagnation of the bile.

The treatment can often be best carried out at one of the spas, but good results may be obtained at the patient's home. A half pint to a pint of alkaline water should be taken hot one-half to one hour before breakfast, and a similar amount in the middle of the afternoon; good results may follow smaller amounts one-half an hour before each meal and on retiring at night. It is wise to begin with small doses and gradually increase; the amount and the frequency of administration should be gauged by the result, particular attention being paid to free evacuation of the bowels. The saline cathartics, magnesium or sodium phosphate, may be used, aided by injections of hot or cold water.

Many drugs have been advocated but few have withstood the test of experience. Cholagogue properties have been ascribed to many that need not be mentioned; salicylic acid and its preparations and preparations of the bile itself are efficacious. Salicylic acid seems to augment the flow of bile by stimulating its production, and since it also possesses antiseptic properties and is excreted with the bile, it exerts a useful influence on the biliary infection. Salicylic acid may be combined with sodium bicarbonate, oleate or benzoate; or the salicylates may be given. Crowe[1]

[1] *Johns Hopkins Hosp. Bull.*, 1908, **19**, 109.

demonstrated that hexamethylenamine is excreted in the bile and the pancreatic juice, directly through the wall of the gall-bladder, etc., and that, especially after single large doses (75 gr. within twenty-four hours), it appears in the bile in such amount as to exert a decided bactericidal action. Ox-gall also stimulates the secretion and outpouring of bile, and thus favors drainage of the biliary tract; it should be administered as salts of the bile acids, such as sodium glycocholate (10 to 15 gr. daily). Ammonium chloride is sometimes useful for its effect upon inflamed mucous membranes; by promoting the free flow of thin bile it may assist in flushing the biliary tract.

Surgical Treatment.—In many cases medication is altogether inefficacious, and resort must be had to surgical intervention. The important question to decide is, When should an operation be undertaken? In many cases the question of early operation scarcely admits of discussion. These are cases in which there is acute cholecystitis (with or without cholangitis —jaundice), with evidences of severe infection, and in which the symptoms and local signs, instead of abating, become more pronounced: these comprise cases of acute cholecystitis in which impending if not actual infection of the hepatic ducts is not unlikely. The risk attending the progress of the disease in such cases is more than the hazard of the operation; indeed, without operation many unquestionably terminate fatally. Happily, however, most of the acute infections of the biliary tract subside spontaneously or under treatment. In general, it is much wiser that the acute manifestations should subside without operation—which, should it be deemed desirable later, may then be undertaken with much more reasonable hope of ultimate success. The use of non-surgical drainage, both pre- and postoperatively, will better prepare the operative field, reduce the surgical risk, and tend to prevent secondary cholangitis. Indeed, a course of non-surgical drainage may so improve the patient as to make the need of operation less evident or less urgent.

Operation, although not always necessarily immediate, is indicated in all cases of persistently enlarged gall-bladder, whether due to simple hydrops, empyema, or gall-stones.

The question of when to operate in cases of gall-stones that have become or have been active must be decided in each individual case; but one should bear in mind that, as a rule, it is not the many stones in the gall-bladder that do the most damage, but the one or two stones that get into the ducts; that the special risk attending operations for gall-stones increases with delay; and that whereas gall-stones are readily removed from the gall-bladder, their removal from the ducts is commonly attended with serious difficulties and is sometimes impossible. The time of election for operation, therefore, is before the stones have entered the ducts. If the gall-bladder is enlarged and the stones have given warnings—local discomfort and distress unrelieved by duodenal tube drainage—operation should be undertaken. Two, certainly three, attacks of gall-stone colic should be looked upon as a positive indication for operative intervention, although spontaneous and permanent arrest of symptoms, amounting to a genuine cure may occasionally follow repeated attacks of colic. In the event of hesitation by the patient, the patho-

logical changes and the likely course of the disease should be explained, and he should be required to make the decision for or against operation.

In impaction of a gall-stone with chronic jaundice operation is called for. The risk of gall-stone operations is the risk of delay, since with delay serious infections of the biliary tract supervene, the tendency to hemorrhage increases with the persistence of the jaundice, the general nutrition of the patient fails, he becomes less able to withstand the operation, and stagnation of the bile leads to dilatation of the ducts and seriously compromises the functional activity of the liver cells. The decision as to the time of operation must be made for each individual patient, but there scarcely seems any advantage attending a delay beyond one or two weeks, and this, too, in full knowledge of the fact that some patients have recovered without operation after a much longer period. Preoperative preparation of the jaundiced patient by a few days of continuous nonsurgical drainage will materially lessen the surgical risk. Finally, operation is indicated in those obscure cases in which with reasonable certainty the presence of pericholecystic, perigastric, or periduodenal adhesions may be surmised.

In each of the foregoing classes of cases operative measures attain that which is impossible of attainment, or attainable only with difficulty by medicinal measures—whence surgical measures find their justification. They find additional justification in the fact that early intervention tends to prevent the development of certain complications and sequelæ. An operation, however, should not be lightly undertaken in persons suffering with disorders of nutrition, or in those with faulty kidneys, etc. The risk is too great and the recuperative power of the patient too much reduced to expect from operation a great deal more than can probably be attained by well-directed medicinal, hygienic, and dietetic treatment, aside from the fact that in the one instance the patient will remain alive, although indisposed, while in the other he may be much longer dead. Finally, the fact that the operative results are not always what were hoped for is not in itself a contraindication to operation; on the contrary, these untoward results are often due to the fact that in long-delayed cases the anatomical lesions are almost if not quite irremediable by any means at our command.

CARCINOMA OF THE GALL-BLADDER AND BILIARY DUCTS

Carcinoma of the gall-bladder and biliary ducts may be primary or secondary. The secondary cases are of comparative rarity and of little clinical importance; usually the lesions constitute a subordinate part of a general carcinomatosis. The metastases in the gall-bladder consist of nodules of varying size, rarely of a more diffuse infiltration on or just beneath the peritoneum; the mucosa is seldom involved. The biliary ducts are much less rarely implicated, although occasionally invaded from without in carcinoma of the pancreas, stomach, etc. These secondary growths form usually only an insignificant part of the general metastasis, and can scarcely be recognized clinically, unless the irregular, nodular enlargement of the gall-bladder becomes conspicuous, or the

cystic or common bile duct becomes obstructed. In the first of these two events hydrops of the gall-bladder may ensue, and in the other, chronic jaundice, which only with difficulty can be distinguished from other types of chronic jaundice.

Primary carcinoma of the gall-bladder and the biliary ducts is three to four times as common in the gall-bladder as in the biliary ducts. At the necropsy it is often difficult to determine definitely where the lesion began, but it seems desirable to exclude from the cases of primary carcinoma of the biliary ducts those in which the new growth developed from the fine intrahepatic ducts; these are virtually cases of carcinoma of the liver. When the extrahepatic ducts are involved, the disease may spread along the ducts and involve the gall-bladder, the pancreas, the omentum, etc., or primary disease in any of these structures may spread to the ducts. Thus carcinoma of the gall-bladder and of the cystic duct is virtually one disease, although sometimes it may be differentiated; carcinoma of the gall-bladder and of the pancreas may spread to the biliary ducts, and *vice versa;* carcinoma of the gastro-hepatic omentum may originate in the biliary ducts; and in some cases so widespread is the new growth and so dense and cicatricial the adhesions that carcinoma, if at all suspected, can only with the greatest difficulty be referred to its true point of origin. In some cases the condition is thought to be inflammatory, and only a microscopic examination will disclose its real nature. Rare cases of sarcoma of the gall-bladder and biliary ducts have been described.

Etiology.—*Primary carcinoma of the gall-bladder* is a fairly common disease. In 1889 Musser[1] collected 100 cases; in 1901 Fütterer[2] collected 268 cases. The disease is much more common in women than in men; in Musser's cases there were 75 females to 23 males (3 to 1); in Fütterer's, 204 females to 52 males (4 to 1). It is especially prevalent in advanced life; the average age in Fütterer's cases was fifty-eight years. An important etiological question is the interpretation of the relationship between carcinoma of the gall-bladder and cholelithiasis. Frequently they are associated: in 69 per cent. of the cases (Musser), in 78 per cent. (Fütterer), in 81 per cent. (Winton), in 85 per cent. (Zenker), in 91 per cent. (Courvoisier), in 95 per cent. (Siegert, Keen), and in 100 per cent. (Janowski). Rolleston, from a study of many statistics, estimates that carcinoma of the gall-bladder occurs in from 4 to 14 per cent. of cases of cholelithiasis.

Leitch[3] has studied the incidence of gall-bladder cancer associated with gall-stones. He states that the reported incidence of cancer with gall-stones ranges from 0.6 per cent. to 30 per cent. Leitch estimates that over 10 per cent. of adults have gall-stones and that 5 per cent. of these develop carcinoma of the gall-bladder.

Carcinoma of the extrahepatic biliary ducts has been attentively studied by Rolleston, who has collected 90 cases. Of 85 of these, 50 (58.8 per cent.) occurred in males and 35 (41.1 per cent.) in females. In 58 (69.8 per cent.) of 83 cases the patient was beyond fifty years of age; extremes

[1] *Boston Med. and Surg. Jour.*, 1889, **121**, 525, 553, 581.
[2] *Ueber die Aetiologie des Carcinoms*, 1901.
[3] *Brit. Med. Jour.*, 1924, ii, 451.

of age were eighty-one years (a woman) and twenty-nine years (a man). In contrast with carcinoma of the gall-bladder, gall-stones are much less frequently associated with carcinoma of the biliary ducts; in 67 of Rolleston's cases, gall-stones were present in 23 (34.3 per cent.).

Carcinoma of the ampulla of Vater (choledochopancreatic duct) also has been studied by Rolleston, who has collected 19 cases; of these, 14 were in males and 5 in females; the average age was 55.2 years in both sexes, the extremes being thirty-four and eighty-one years. Since gall-stones were present in only 2 of the 19 cases, it is likely, as Rolleston maintains, that there is no relationship between gall-stones and carcinoma of the ampulla of Vater.

Crohn[1] has studied these conditions by duodenal tube methods. He reports 8 cases and states that we can recognize six principal points from which a new growth in this vicinity can originate, namely, the head of the pancreas, the papilla of Vater, the common bile duct (these three being the most common), the ampulla of Vater, the duct of Wirsung, and the duodenal mucosa (these being much less frequent).

Pathology.—*Carcinoma of the gall-bladder* most commonly involves the fundus, which is said to be due to the fact that, being the most dependent part, the fundus is especially subject to irritation by a gall-stone; second in point of frequency of growth is the neck of the gall-bladder or the beginning of the cystic duct—attributed to the attrition of impacted gall-stones; third, the growth may be situated anywhere in the gall-bladder or involve the entire organ. In 45 of Fütterer's cases the growth was situated at the fundus in 17, at the neck in 13, in the posterior wall in 8, and on the anterior wall in 7. Two types of growth may be distinguished: that which projects into the lumen, a villous or cauliflower-like growth, and is believed by some to originate as a papilloma, and that which infiltrates the wall of the gall-bladder, and is believed by some to originate as an adenoma. In reality the two varieties cannot be differentiated; the one growth may exhibit appearances significant of both types. Extension to the liver ensues in more than 50 per cent. from direct growth into the adjacent liver, or by extension along the biliary ducts, by way of the lymphatics in the wall, or through the lumen of the ducts. Adhesions between the carcinomatous gall-bladder and adjacent organs are common. Miller[2] believes that chronic inflammation associated with gall-stones produces either a papillomatous outgrowth, or an original downward ingrowth with metaplasia, and that these initial tendencies determine the subsequent course of the tumor, producing three important forms (*a*) villous, papillomatous, or fungating, (*b*) gelatinous, and (*c*) diffuse, flat, infiltrating carcinoma. The papillo-adenomas are usually of large size, extend downward along the cystic and common ducts and invade the liver only late in the disease, whereas the second and third types involve the lymph nodes and peritoneum at an earlier stage. Sarcoma is uncommon and occurs as a result of long-continued inflammation (often associated with stones) developing into two main forms, (*a*) as an overgrowth of smooth

[1] *Am. Jour. Med. Sci.*, 1914, **148**, 839.
[2] *Boston Med. and Surg. Jour.*, 1924, **191**, 1074.

muscle and (*b*) as an inflammatory new growth of connective tissue and bloodvessels. Spindle cell sarcoma has been reported.

In the 90 cases of *carcinoma of the biliary ducts* collected by Rolleston the situation of the growth was as follows: In the common bile duct, 34 (lower end 23, midpart 11); at the junction of the common bile duct, cystic duct, and common hepatic duct, 27; in the common hepatic duct, 19; in the right or left hepatic ducts, 3 (the last two classes constitute the so-called juxtahepatic cases); in the cystic duct, 6; and in the cystic duct and the lower end of the bile duct, 1. Usually the growth infiltrates the wall of the duct and forms a firm annular stricture; occasionally it extends in the wall of the ducts for a considerable distance, and transforms them into thick rigid tubes; in some instances the growth projects considerably into the lumen, and produces obstruction rather than annular stricture. Complete biliary obstruction is produced, due in part probably to added muscular spasm, since after death the stricture does not always appear to be absolutely impervious.

Above the growth the biliary ducts are dilated, sometimes to such an extreme degree as to allow a finger or a thumb to be introduced. When the growth is in the common bile duct the gall-bladder is distended, except it be bound down and retracted on itself in consequence of former cholelithiasis; when the growth is in the common hepatic duct, the gall-bladder is nearly always small, except in the rare instances in which it may be distended with mucus from concomitant obstruction of the cystic duct, or may be occupied by a number of gall-stones; when the growth is situated at the junction of the cystic, hepatic, and common bile ducts, the gall-bladder, as a rule, is not enlarged, but from irregularities and variations in the degree of obstruction to the different ducts, corresponding differences in the gall-bladder are met with.

The liver, in addition to dilatation of the biliary ducts, reveals atrophy of the parenchymatous cells, focal necrosis, relative increase in the connective tissue, and in the event of chronic infection of the biliary ducts pericholangitic fibrosis, and occasionally true cirrhosis; suppurative lesions may follow acute infections. Usually the growth does not invade adjacent tissues or organs, but it may grow into the pancreas, liver, or portal vein. Metastases are uncommon, largely because of speedy death; they are most common in the liver (13 of 57 of Rolleston's cases); but they occur also in the regional lymphatic glands, the peritoneum (causing ascites), etc. Miller believes that *carcinoma of the extrahepatic biliary ducts* is of considerable importance because relatively small carcinoma will cause an obstructive jaundice at an early period and because the progress of such cases is rapidly fatal. It is also of interest because there is a notable absence or infrequency of associated gall-stones and because the disease is more common in males than in females, which ratio is usually reversed in primary carcinoma of the gall-bladder. There are three main forms: (*a*) Villous, (*b*) nodular, encircling and constricting duct, and (*c*) diffuse growth along the duct. The usual cellular type is the adenocarcinoma. Mayo-Robson notes that when the carcinoma originates in the cystic duct near the neck of the gall-bladder, the function of the pylorus is frequently disturbed giving rise to symptoms suggestive of carcinoma of the stomach.

Carcinoma of the ampulla of Vater (choledochopancreatic duct) should be distinguished from carcinoma of the termination of the common bile duct, of the termination of Wirsung's duct, and of the duodenal surface of the biliary capillaries. The growth tends to obstruct the orifice of Wirsung's duct and thus to produce dilatation of the intrapancreatic ducts and chronic interstitial pancreatitis; the same result may ensue upon extension to the orifice of Wirsung's duct of carcinoma of the lower end of the common bile duct.

Symptoms.—The onset of the symptoms referable to *carcinoma of the gall-bladder* may or may not be preceded by symptoms due to associated disease—cholecystitis and cholelithiasis. Some patients complain for years of dyspepsia, but which careful inquiry shows to be in reality chronic cholecystitis with perhaps pericholecystic adhesions; in other cases there is a more or less clear history of gall-stones. There may have been many attacks of obvious colic (with or without jaundice), or there may have been few, perhaps only one, remote and ill-defined attacks; the gall-stones have remained latent as perhaps occurs in most cases.

The onset of the symptoms is insidious, and usually the disorder makes considerable progress before its true nature is suspected. The patient, usually an elderly woman, complains of ill-defined gastric symptoms, with more or less severe, sometimes colicky, pain. These are usually ascribed to dietetic indiscretions; in some cases, however, the pain is so severe and perhaps referred to the right of the median line, and some local tenderness is found on examination, that the symptoms are put down to cholecystitis or cholelithiasis. The attack subsides, perhaps it recurs; the patient is thought to be the subject of cholelithiasis, and for some time the symptoms may be quite indistinguishable from cholecystitis with pericholecystic adhesions.

Soon, however, the gall-bladder may enlarge, jaundice supervenes, or the general health becomes impaired. An obvious palpable and often visible enlargement of the gall-bladder develops in more than half of the cases; in itself it is not significant of carcinoma, since it resembles that due to cholelithiasis or obstruction of the cystic duct; in advanced stages, however, it may become quite irregular and nodular, whereupon it is much more significant of new growth. Usually it reveals its attachment to the liver by moving with it during the phases of respiration and showing no intervening area of tympany; sometimes it is fixed to the abdominal wall by adhesions, and it may be quite tender. In some cases the tumor is the first obtrusive evidence of the disease. Miller states that the history of symptoms in cases of carcinoma of the gall-bladder can be divided into three groups. (1) The patients have had recurrent gall-stone colic and the picture suddenly changes to that of malignancy; (2) a group in which the malignant cachectic features occur in patients complaining of chronic dyspepsia; (3) a group of patients whose first symptoms (loss of weight, cachexia, pain or distress over gall-bladder, tumor) occurred within a period of one year. Such cases are usually inoperable when they reach the surgeon. Of 2631 gall-bladder operations done over a thirty-year period at the Massachusetts General Hospital, there were 63 instances (2.4 per cent.) of primary

carcinoma of the gall-bladder or bile ducts. Gall-stones were found in only 36 per cent. of 663 cases. As to symptoms noted in this group of cases, Miller records that 42 had indigestion of a vague type, 32 jaundice at some time, 20 had attacks of gall-stone colic, 20 had suffered loss of weight; 9 were aware of a tumor in the right side, and 5 had been previously operated upon for gall-stones. On hospital admission the following features were noted. A palpable mass in 33, jaundice in 26, and enlarged liver in 26. Miller believes that since 1 to 5 of every 100 patients with gall-bladder disease will develop carcinoma of the gall-bladder, an early cholecystectomy should be the operation of choice.

Jaundice occurs in three-fourths or more of the cases (69 per cent., Musser; 86 per cent., Meurrier); but it is not always due to the same cause. Rarely it may result from duodenal catarrh or catarrhal cholangitis, last a short time and subside; or it may be due to a gall-stone in the common biliary duct, when it is likely to be intermittent and perhaps accompanied by intermittent fever; usually, however, it is due to extension of the new growth into the biliary ducts, or to pressure from without on the extrahepatic biliary ducts. The jaundice in this event is progressive, soon becoming very deep, and it is permanent.

With the progress of the disease the general health becomes impaired; this may be the first noteworthy evidence of its malignant nature. The patient gradually loses weight and strength, becomes anemic, and presents the manifestations of cachexia. Dyspeptic symptoms develop, or become aggravated, in which event they may be due not only to the original cholecystitis or cholelithiasis, but also to an associated pyloric obstruction. Occasionally the carcinoma may invade the colon, giving rise to obstruction, or to a cholecystocolonic fistula. In other cases the gall-bladder forms adhesions with the peritoneum, and ultimately perhaps perforates thereinto, giving rise to a localized or more generalized peritonitis. *Ascites* occurs in about one-fourth of the cases, and is due most commonly to associated perihepatitis or peritonitis; rarely it may be due to obstruction of the portal circulation by the original growth or secondarily involved glands. Ultimately in the cases with jaundice the patient develops a condition attributed to hepatic insufficiency (hepatic toxemia, cholemia) and dies with asthenia, delirium, and coma. In the absence of jaundice, the patient generally dies of asthenia. The disorder may run a fatal course within six months.

The symptoms of *carcinoma of the extrahepatic biliary ducts* are usually insidious. There may be antecedent dyspeptic symptoms of variable duration, and ill-defined complaints of disturbance of the general health. Jaundice is usually the first noteworthy symptom. In most cases it develops gradually; occasionally rather suddenly, imitating catarrhal cholangitis or a gall-stone arrested in the common duct. The jaundice is progressive and permanent; it soon becomes extreme, and biliary pigments disappear from the stools and appear in the urine. Pain in the right hypochondrium or the epigastrium is quite common, and is usually dull in character; sometimes it is severe, suggesting gall-stone colic, but it is more likely due to spasmodic contraction of the gall-bladder against an obstruction. Obstruction to the flow of bile results in enlarge-

ment of the gall-bladder, which is palpable in one-half or more of the cases as a smooth pear-shaped swelling. Metastasis occurs in about one-half of the cases, but the nodules are usually small and not palpable during life. Should metastasis occur, it may lead to ascites. Infection of the biliary ducts and suppurative cholangitis may ensue. The symptoms of *carcinoma of the ampulla of Vater* are practically identical with those of carcinoma of the common bile ducts.

Diagnosis. Carcinoma of the gall-bladder is suggested by a history of ill-defined dyspeptic symptoms, perhaps interrupted by definite signs attributable to cholelithiasis or cholecystitis; pain in the right hypochondrium; jaundice; hard, nodular, and progressive enlargement of the gall-bladder; and gradual loss of flesh and strength. Attention to the sequence and grouping of the symptoms would probably permit of the diagnosis before the onset of jaundice, which is not a phenomenon of carcinoma of the gall-bladder itself, but of extension of the disease; but in the great majority of cases jaundice supervenes before the patient is thought to be seriously ill. Carcinoma of the biliary ducts is suggested by insidious but persistent and progressive jaundice, smooth, uniform enlargement of the gall-bladder, loss of flesh and strength, in a patient about or over fifty years of age, without determinable cause of jaundice.

Carcinoma of the gall-bladder and biliary ducts is simulated by a number of other conditions, such as chronic cholecystitis and cholelithiasis, carcinoma and other tumors of adjacent organs. Chronic cholecystitis and cholelithiasis are, in most cases, antecedent to carcinoma of the gall-bladder, so that it is extremely difficult if not impossible, in most cases, to say when the new growth begins. The diagnosis is favored by the detection of progressive nodular enlargement of the gall-bladder; but in many cases the carcinoma develops when the chronic inflammatory process has lasted a long time and caused much thickening and many adhesions to adjacent viscera, so that should the growth not attain at least moderate dimensions, no specially noteworthy enlargement of the gall-bladder becomes apparent. The diagnosis in these cases awaits the development of cachexia or of metastasis.

In the early stages, carcinoma of the gall-bladder may sometimes be distinguished from carcinoma of the liver, by the absence of jaundice, due to limitation of the new growth to the gall-bladder; but in the more advanced stages, when the disease is more widespread and involves the liver more or less extensively, the diagnosis may be quite impossible.

Carcinoma of the head of the pancreas, causing jaundice, can scarcely, if ever, be distinguished from carcinoma of the biliary ducts, aside from the fact that carcinoma of the head of the pancreas is much more common, the pain is more likely to be epigastric than hypochondriac; a tumor deep in the epigastrium (close to the vertebræ) may sometimes be felt.

In the early stages, carcinoma of the gall-bladder and of the biliary ducts may sometimes be distinguished by the absence of jaundice and the presence of an enlarged and nodular gall-bladder, and the early presence of jaundice and a smooth and uniform enlargement of the gall-bladder. Later, when jaundice occurs in carcinoma of the gall-

bladder, the jaundice being due to extension to the ducts or pressure by enlarged glands on the ducts, the differences are slight.

Carcinoma of the ampulla of Vater closely resembles carcinoma of the biliary ducts. Rolleston states that there are a few points of difference: in carcinoma of the ampulla (1) jaundice is said to be often intermittent, the feces becoming bile-stained, and the icteric tint of the skin diminishing or even passing off in the earlier stages when the obstruction is possibly valvular, or partly due to spasm of the ducts set up by the irritation of the growth. Confusion is apt to arise between carcinoma of the ampulla and carcinoma of the duodenal surface of the papilla, in which jaundice is by no means constant; (2) intermittent hepatic fever and suppurative cholangitis are apt to occur; (3) diarrhœa is more often seen than in carcinoma of the ducts.

Prognosis.—Carcinoma of the gall-bladder and the biliary ducts is necessarily fatal, unless it can be removed by surgical intervention. Under non-surgical treatment patients seldom live more than six months from the onset of serious symptoms. The mortality is high also under surgical treatment, many patients succumbing to the operation or to postoperative hemorrhage; in others the growth is too extensive to be removed; in others, recurrences ensue or a fistula persists.

Treatment.—The treatment is essentially surgical. Even the suspicion of malignant disease is an indication for operation; the hazard of the operation is less than the risks of delay. Since carcinomas occur in from 4 to 14 per cent. of cholelithitic subjects, the operative treatment of cholelithiasis naturally tends to reduce the incidence of carcinoma of the gall-bladder. Some surgeons believe that it is safer to operate upon all gall-stone cases because between 5 and 10 per cent. of all gall-stone carriers so operated have shown coincident cancer of the gall-bladder, presumably produced by stone irritation, and that by removing the stones, the cancer risk is avoided. Such reasoning might be logical until it is remembered that the operative mortality risk when averaged throughout the country is likewise between 5 and 10 per cent.; therefore, if such a plan were carried out on all gall-stone carriers in order to avoid a cancer death, the cure would be as bad as the disease. Furthermore, some authors pertinently call attention to the fact that if the gall-stone factor in producing gall-bladder cancer is considered so great, why do so many of the gall-stone carriers not operated upon fail to develop gall-bladder cancer. Aside from the removal of the growth, a fistula may be established between the gall-bladder and the intestine in cases of carcinoma of the common duct or of the ampulla of Vater. Apart from operation, the physician's efforts are limited to relieving distress.

CHAPTER XIV

DISEASES OF THE PERITONEUM

By Sir HUMPHRY ROLLESTON, Bart., K.C.B., M.D., F.R.C.P.

Introductory.—The peritoneum is a serous sac of extensive dimensions. In fact, when all its reflections and fossæ are taken into account, its superficial area is but slightly less than that of the skin. In the female it differs from all other serous cavities in that its potential cavity opens indirectly externally through the Fallopian tubes, but in the male it is completely shut off from the exterior.

The peritoneum has remarkable powers of absorption. Thus in a dog or rabbit, fluid equal to 10 per cent. of the body weight of the animal can be absorbed from the peritoneal cavity in half an hour. Fluid and soluble substances are conveyed away by the bloodvessels, while, in addition, the lymphatics, with the aid of phagocytes, carry off insoluble bodies, including microörganisms. It was formerly thought that the peritoneal cavity was in direct communication with lymphatic vessels by open apertures or "stomata," and that it was an appendage of the lymphatic system but Muscatello[1] and MacCallum[2] have shown that the endothelial lining of the peritoneum is everywhere continuous and complete, and that there is no actual communication between its cavity and the lymphatics.

The peritoneum covering the under surface of the diaphragm differs from the rest of the peritoneum in having a number of depressions or pits, formerly described as stomata or lacunæ, opening into the lymphatic vessels, but in reality closed by a continuous layer of endothelial cells. These cells, however, by phagocytic action, play an important part in the absorption of solid particles, and Buxton[3] has shown that bacteria injected into the peritoneal cavity of animals are immediately absorbed by the lymphatics of the diaphragm and reach the general circulation in a few minutes. When the endothelial layer of the peritoneum is intact, microörganisms are probably not absorbed by the bloodvessels, but damage to these delicate cells allows rapid absorption of bacteria to take place, and hence septicemia may result. The preservation of the endothelial lining of the peritoneum is therefore of the greatest importance.

In health, secretion of fluid, mainly by the great omentum, into the peritoneal cavity and its absorption therefrom are so evenly balanced that there is just enough fluid to keep the serous surfaces moist and free from friction. In morbid conditions this state of equilibrium is disturbed and the amount of fluid may become excessive—*ascites*. The

[1] *Virchow's Archiv.*, 1895, **142**, 327.
[2] *Johns Hopkins Hosp. Bull.*, 1903, **14**, 105.
[3] *Jour. Med. Research*, Boston, 1907, **16**, 25.

pathological effects produced by the drying of the peritoneum are not so well known. It has been shown experimentally that it diminishes the power of absorption, and in practice it is clear that it impairs the vitality of the peritoneum, since it readily splits or tears on handling. The small amount of fluid also plays an important part in the defense of the peritoneum against infection by exerting a bactericidal action.

The lymphatic trunks draining the peritoneal cavity run up into the thorax, especially to the anterior mediastinal glands (Durham). The peritoneum covering the diaphragm and the omentum is particularly active in this process of absorption, removing not only inert bodies but microörganisms from the peritoneal cavity; the omentum is, further, a most important factor in preventing peritonitis, since it removes microörganisms from the abdominal cavity before they can exert their pathogenic effect locally. Thiele and Embleton[1] found that absorption by the lymphatics and the passage of microbes to the anterior mediastinal glands were much slower and less important than by the bloodvessels. Bolton[2] while confirming the view that the peritoneal cavity is principally drained by the lymphatics into the anterior mediastinal glands admits the direct passage from the peritoneal cavity into the blood of bacterial poisons. The omentum is apt to attach itself to any inflamed organ or possible source of infection, and thus to localize the peritoneal infection. The absorptive powers of the peritoneum are diminished by the backward pressure of chronic venous engorgement, probably by lymphatic obstruction, and by less vigorous peristaltic and diaphragmatic movements.

The visceral peritoneum is quite insensitive to pain, while the parietal layer is extremely sensitive. Excessive peristalsis and dragging on the mesentery cause pain because traction is thus exerted on the parietal peritoneum which is supplied by the nerves of the abdominal wall. The deep tenderness on pressure in peritonitis is due to inflammation involving the parietal layer, and tenderness in inflammatory conditions of the stomach, appendix, etc., depends on lymphangitis and extension of inflammation to the parietal peritoneum.

Comparison of the Peritoneum with Other Serous Membranes.—Like the other serous membranes the peritoneum is extremely resistant to the spread of inflammation from the tissues of the body wall covering it. It, however, is often affected, together with the adjacent pleuræ and pericardium, and infection and inflammation readily spread through the diaphragm. This associated inflammation is spoken of as polyorrhomenitis, or multiple serositis, and may be acute or chronic, but is more often localized or at least partially circumscribed than universal.

In common with the other serous membranes the peritoneum suffers mainly from infections derived from the organs which it surrounds and protects. Thus, like the lungs and synovial membranes, it is often affected by tuberculosis, because that form of infection commonly attacks the intestines. While unlike the pericardium, it may be regarded as immune to acute rheumatic inflammation, which is not recognized as attacking any of the organs covered by the peritoneum, with the possible

[1] *Proc. Roy. Soc. Med.*, 1914, **7**, (Path. Sect.), 69.
[2] *Jour. Path. and Bacteriol.*, Edin., 1921, **24**, 429.

exception of the vermiform appendix. Like the other serous membranes, it may be infected by the blood-stream, but hematogenous infection of the peritoneum is subordinate in importance to the local origin of infection. In common with other serous membranes inflammation of the peritoneum has a great tendency to lead to adhesions.

Immunity.—The natural resistance of the peritoneum varies in individuals. Different parts of the peritoneal cavity probably differ in their power of resistance; the pelvic peritoneum is thicker in women than in men, and it is possible that this has some influence in its comparative immunity to infection. An attack of peritonitis leaves thickening of the affected area, and thus may to some extent account for the increased resistance to infection which a past attack confers.

ASCITES

Ascites is the presence of free fluid in the peritoneal cavity, and is the counterpart of a pleural effusion. The name hydroperitoneum indicates that the fluid effusion is not manifestly due to inflammation. The presence of fluid in excessive amounts in the peritoneal cavity may depend on the passage of fluid in increased quantities into the sac, the rate of absorption failing to keep pace with this; or on interference with the normal process of absorption, the secretion of fluid into the cavity remaining normal or being increased. The passage of increased amounts of fluid into the peritoneal cavity mainly depends on changes in the endothelial cells of the peritoneum brought about by poisons; this process occurs in inflammation, and is then spoken of as an exudation. When the action of poisons cannot be assumed and the ascites appears to be the result of increased venous or lymphatic pressure—passive or mechanical effusion—the process is spoken of as a transudation. It is obvious that these two processes overlap; thus, passive venous engorgement, by interfering with the vitality of the endothelium, will produce changes analogous to those wrought by poisons.

Etiology.—The causes of ascites in the order of their importance are:

1. *Backward pressure* from tricuspid regurgitation may give rise to copious ascites. In 224 cases in which ascites to the extent of a quart or more was found after death, 89 (or 40 per cent.) were due to various forms of heart disease (Cabot[1]). Although in many of such instances chronic peritonitis may be the determining cause of ascites, this is not always so. In some cases the brunt of the backward pressure seems to fall on the hepatic veins, with the result that there is ascites without œdema of the feet. This condition, which has been called hepatic asystole, may imitate cirrhosis of the liver. In some cases of adherent pericardium there is a high grade of nutmeg liver, ascites, and little chronic peritonitis. The adherent pericardium may be the result of rheumatic fever, or be tuberculous; in some cases the tuberculous nature is only revealed by microscopic examination. Pick[2] described *pericarditic pseudocirrhosis*, but doubt has been cast on its existence as a distinct

[1] *Am. Jour. Med. Sci.*, 1912, **143**, 1.
[2] *Ztschr. f. klin. Med.*, 1896, **29**, 385.

morbid entity; it is advisable to keep an open mind on this difficult question, but probably some of the cases so described may be included under the heading either of advanced nutmeg liver or of chronic peritonitis associated with adherent pericardium. Acute cardiac failure gives rise to a small amount only of ascitic effusion, which in itself is of no clinical importance. Stricture of the hepatic veins, or thrombosis of the inferior vena cava occluding the orifices of the hepatic veins, may give rise to marked ascites.

2. *Chronic Peritonitis.*—(*a*) Simple, either universal or diffuse, which does not involve the whole of the peritoneum, but is more or less limited to part of the abdominal cavity, especially the upper half over the liver and spleen. (*b*) Associated with infection of the peritoneum by malignant disease. It may be associated with so-called "cirrhosis of the stomach," which is generally regarded as carcinomatous. (*c*) In rare instances innocent tumors, such as ovarian cystadenomas and fibromas, and uterine fibromyomas, set up sufficient chronic peritonitis to cause ascites. Papilloma of the ovaries may give rise to multiple implantation growths on the peritoneum, which irritate the peritoneum and so cause ascites. (*d*) Tuberculous peritonitis. Simple or "idiopathic" ascites, especially in young girls, is in many cases tuberculous.

3. *Cirrhosis of the Liver.*—Hypertrophic biliary or Hanot's cirrhosis, which is comparatively rare, is either not complicated by ascites or only at a very late stage, and then to a slight degree. In portal or common cirrhosis, ascites is met with in 80 per cent. of the cases fatal from the effects of the disease. It may be due to the cirrhosis alone, and is then a late or terminal phenomenon, and rarely requires tapping more than twice. Ascites may be merely associated with cirrhosis and be caused by chronic simple or tuberculous peritonitis, or by cardiac failure. In these cases numerous tappings may be necessary.

4. *Other Morbid Conditions of the Liver.*—Hepatic syphilis is often associated with chronic perihepatitis and peritonitis; but as it cannot always be proved that the accompanying ascites is set up in this indirect manner, syphilis of the liver may be regarded as a cause of ascites. Out of 56 cases of hepatic syphilis, ascites occurred in 23, or 41 per cent. (T. McCrae[1]). A lardaceous liver in rare instances, and then usually in children, appears to be responsible for ascites. In malignant disease of the liver ascites is common; in most cases the growths project from the capsule and by irritating the peritoneum induce ascites; but growths may press upon or invade and block up large branches of the portal vein inside the liver, especially in primary carcinoma with cirrhosis. In some cases new growth may block up the capillaries in the liver so widely as to produce marked portal obstruction and ascites, as is well shown in secondary melanotic sarcoma of the organ (Hektoen and Herrick[2]). Ascites may occur in hepatic and abdominal lymphadenoma, and is explained in the same way as in malignant disease. From an analysis of 100 cases of ascites in Egypt, Phillips[3] finds that 30, and

[1] *Am. Jour. Med. Sci.*, 1912, **144**, 625.
[2] Ibid., 1891, **116**, 255.
[3] *Records of the Egyptian Government School of Medicine*, 1904, **2**, 47.

possibly 52 per cent., of these cases were due to the effects of chronic malaria in the liver and spleen.

Perihepatitis is considered under Simple Chronic Peritonitis.

5. *Thrombosis of the portal vein* is rare but usually causes a rapid and extensive ascitic effusion, which speedily recurs after tapping. Pressure on the portal vein may, but does not necessarily, produce ascites.

6. In universal *renal dropsy* the peritoneum may contain free fluid.

7. *Inflammation of the Peritoneum.*—Subacute and acute inflammation of the peritoneum will, of course, give rise to an effusion.

In addition, rupture of hydatid, ovarian, or other cysts may give rise to free fluid in the peritoneal cavity; in the case of ruptured hydatid cysts, absorption will, as a rule, rapidly lead to its removal. Rupture of lymphatic vessels or lacteals will cause a chylous effusion. Effusions of bile (choleperitoneum) and of pure blood (hemoperitoneum) are referred to elsewhere.

Pathology.—The *morbid anatomy* of ascites is, except for the mechanical effects due to abdominal distention, that of the underlying cause, such as chronic peritonitis, cirrhosis, and new growth. Portal obstruction when present increases the anastomotic channels between the systemic and the portal veins. The veins of the peritoneum, especially at the back of the abdomen, become manifestly enlarged; veins in any adhesions become prominent, and the parumbilical vein in the falciform ligament may reach a large size; the veins at the lower ends of the œsophagus and rectum also become tortuous and dilated. The abdominal muscles become stretched and atrophied; the diaphragm is pushed up, and may show hypertrophy from increased work. Upward displacement of the diaphragm may compress the lower lobes of the lungs. The presence of adhesions may produce encysted or loculated ascites.

The characters of ascitic fluid vary according to the causes at work. Thus, when there is inflammation of the peritoneum (exudates) the specific gravity and amount of contained protein are higher than in ascites associated with backward pressure (transudates). Serous ascitic fluid is clear, transparent, and greenish or faintly yellow in color. The reaction is alkaline, and the specific gravity under 1.012 in mechanical effusions, or hydroperitoneum, and 1.018 or higher in the exudations in subacute or chronic peritonitis. The amounts of solids and contained proteins vary. In simple effusions due to renal disease there may be only 0.3 per cent. or less of protein, while in inflammation the amount may be 4 per cent. In some instances, especially of ascites associated with rupture of ovarian cystadenomas, the fluid is sticky from the presence of pseudomucin. Occasionally cholesterin, urea in traces or in larger amounts, and various extractives are present. After repeated tappings the character of the effusion may alter, and from added inflammatory changes in the peritoneum be of higher specific gravity and show a higher percentage of proteins.

In jaundiced patients the ascitic fluid contains bile pigment. A blood-stained or hemorrhagic ascites may occur in (1) intra-abdominal malignant disease, from leakage; this is rare in carcinoma and is more often associated with vascular or hemorrhagic sarcomas or endotheliomas.

(2) Some cases of hepatic cirrhosis; here it is usually the result of trauma, such as rupture of a dilated vein in the peritoneum or in vascular adhesions, either from traction or from direct injury by the trocar. As a rule, the blood-stained character of the effusion is seen not at the first but at a subsequent tapping. (3) Ascites is blood-stained in about one-fourth of the cases associated with ovarian cysts, and in about one-sixth of the cases of ascites associated with uterine fibromyomas (Cabot[1]). (4) Red-blood corpuscles have been found exceptionally on microscopic examination of the ascitic fluid in tuberculous peritonitis (Grenet and Vitry[2]). (5) A certain amount of blood-stained fluid, but rarely sufficient to be recognized clinically, may be associated with strangulated hernia, volvulus, infarction of the intestines, and hemorrhagic pancreatitis. Sometimes the ascitic fluid clots spontaneously on standing.

The *cells* seen on microscopic examination vary in the different kinds of ascites. In ascites due to mechanical causes, *e. g.*, heart disease and hepatic cirrhosis, endothelial cells are predominant; in tuberculous peritonitis small lymphocytes are present in a high percentage, but in some cases of cirrhosis without any evidence of tuberculosis there is a predominance of lymphocytes, and this is also found in the ascites due to intra-abdominal syphilis and malignant disease; and in other infections the predominant form of cell is the polymorphonuclear leukocyte. (For the cytology of ascites associated with new growth see p. 904.)

Bacteriology.—Ascitic fluid, at any rate, at the first tapping is usually sterile; as a result of paracentesis infection may occur. The colon bacillus and the tubercle bacillus are sometimes present. By his method of inoscopy which consists in examining the clot produced spontaneously or by the addition of salted plasma, Jousset[3] claimed that the tubercle bacillus is present in many cases of ascites in which a tuberculous origin was not suspected, but this has not been generally confirmed.

Chylous, Chyliform, and Milky Non-fatty Ascites.—These three forms are alike in their naked-eye resemblance to milk, and from chemical and physico-chemical investigation Blankenhorn[4] finds that suspended fat, including lecithin and cholesterin, is the sole cause of turbidity in these fluids, protein not playing any part; he therefore suggests that the terms chyliform and pseudo-chylous are misleading and should be discarded.

1. *Chylous ascites* is due to the escape of chyle from the lymphatics or receptaculum chyli. Wallis and Schölberg[5] collected 102 cases in 1910. The fluid is yellowish white, tends to accumulate very rapidly, and its opalescence is constant at successive tappings. The specific gravity is usually about 1.015. The fluid resists putrefaction and does not clot on standing, thus differing from chylous urine. It, however, separates into layers on standing, the fat accumulating on the surface. The distinctive odor of some special article of diet such as butter may be perceptible in it (Straus' sign). The amount of solids is about 4 to 6

[1] *Am. Jour. Med. Sci.*, 1912, **143**, 1.
[2] *Compt. rend. Soc. biol.*, 1903, **55**, 959.
[3] *Arch. de méd. exper. et d'anat. path.*, 1903, **15**, 289.
[4] *Trans. Assn. Amer. Phys.*, 1923, **38**, 230.
[5] *Quart. Jour. Med.*, 1910–11, **4**, 153.

per cent.; the percentages of fat and of protein vary considerably, and may be modified by changes in the diet; there is from 0.4 to 4 per cent. of fat in a very fine state of division; the amount of protein is usually about 3 per cent. Cholesterin is always present, but lecithin occurs only in traces. The reaction is alkaline or occasionally neutral. It accumulates very rapidly. The important characters of true chylous ascites are (1) the finely divided fat, and (2) the absence of leukocytes and other cells showing fatty change.

Chylous ascites is caused by obstruction of the thoracic duct or lymphatic vessels. Pressure from without by tumors or dense adhesions may obstruct the thoracic duct and lead to rupture of the receptaculum chyli or to leakage from its tributaries. Thrombosis inside and infiltration of the walls of the thoracic duct or receptaculum chyli with new growth, or even with tuberculosis, have also been responsible for chylous ascites. Malignant disease, by compressing the lacteals, may so raise the pressure that rupture occurs. Traumatic rupture and rupture attributed to whooping-cough (Wilhelm), to vomiting, and to muscular exertion have been recorded. Chylous ascites may be due to rupture of a chylous mesenteric cyst. It has been met with in only a few cases of filariasis. It should be explained that the free lymphatic anastomosis often obviates chylous ascites when from obstruction due to tumors and other factors it might be expected. A chylous peritoneal effusion may be accompanied by a similar condition in one or both of the pleuræ.

2. *Chyliform or fatty* differs from true chylous ascites in (*a*) that it is due not to leakage of chyle but to the formation of fat in the peritoneal effusion; (*b*) that the globules of fat are large, and (*c*) that cells containing fat are present in the fluid. The opalescence is not, however, always due to suspended fat, for in some instances it persists after all the fat has been removed; there is then a mixture of the two forms of adipose and milky non-fatty ascites. For this reason Wallis and Schölberg group these two forms together as pseudochylous. Chyliform ascites is usually associated with intra-abdominal new growth or with chronic peritonitis, tuberculous or simple. The fat may be derived from the cells of the new growth, or a poison generated in the growth may lead to the production of fat in the leukocytes and other cells suspended in the ascitic fluid. In chronic peritonitis the fat is thought to be formed in the cells in the exudation. In some instances fat in the ascitic fluid may depend on lipemia, which in its turn may be the result of milk diet.

3. *Lactescent, Milky, Non-fatty Ascites.*—In some cases the milky opacity is due not to fat, as it is either absent or present in quantities insufficient to account for the milkiness, but to some other body such as a protein resembling casein, mucinoid bodies, or lecithin. Although resembling chylous and chyliform ascitic fluid to the naked eye in most respects, it does not separate into layers on standing. This form of ascites may occur in intra-abdominal malignant disease and in other conditions. In some instances only the later tappings may show this condition, the earlier ones being clear; or later tappings may be more milky than the first. In such cases it would appear to be in some way related to a low form of chronic peritonitis.

Physical Signs.—The abdomen is enlarged, especially in chronic ascites in which the abdominal muscles have become stretched and atrophied. Measurements of fifty inches are sometimes seen. An extreme grade of abdominal distention was recorded in a woman who had been very frequently tapped and measured eleven feet around the abdomen, which contained forty-seven and a half gallons of fluid after death (Duncan[1]). The abdominal distention is not exclusively due to fluid, but may vary from day to day from flatulency; considerable flatulent distention often precedes the discovery of recognizable ascites. Fetal ascites may be so extreme as to obstruct the birth of the child; the abdomen of a fetus has contained nine pints of fluid (Luker[2]).

In recent and acute ascites the distention is mainly anteroposterior, the abdomen being prominent, especially above the umbilicus, tense, and hard. This is probably due to contraction of the abdominal muscles which are irritated by the distention. In ascites of some duration the muscles become atrophied, flaccid, and thus separation of the recti abdominales and bulging in the flanks result. When, however, ascites comes on in a patient whose abdominal walls are already thin and weak, as in women after repeated pregnancies, the abdomen bulges in the flanks from the outset. The distention is, generally speaking, uniform. But in encysted ascites there is a more or less localized prominence which does not alter in position on movement. There is a positive intra-abdominal pressure (6 to 30 mm. Hg.) in ascites, which diminishes during paracentesis (Pitres,[3] Quirin[4]).

The skin is tightly stretched and may be shiny and present distended veins; in portal obstruction, as in cirrhosis, the large veins are chiefly above and around the umbilicus and in the line of the falciform ligament; but when the obstruction is in the inferior vena cava the veins running from the middle of Poupart's ligament to the costal arch are prominent, and, when considerably enlarged and tortuous, produce the condition spoken of as a "caput Medusæ." This venous dilatation is sometimes due to the pressure of enlarged glands, as in tuberculous or malignant peritonitis, but, as a rule, it is due to the pressure exerted by the ascitic fluid on the inferior vena cava, and therefore disappears after tapping. In cirrhosis both sets of veins may be present, and after paracentesis the "caval" veins disappear while the portal veins persist. The caval veins are most prominent in the lower and lateral part of the abdomen. Occasionally a bruit is audible over these dilated veins in the epigastrium. The umbilicus becomes flush with the surface, after a time everted and tense, appearing as a thin-walled bulla, and has been known to burst when tapping has been unduly delayed. Any existing hernial sacs become distended with fluid. From stretching, the deeper layers of the skin rupture, and in a recent state reddish lines are seen, especially when the abdominal wall is lax after tapping; subsequently these lines appear as crinkled cicatrices, the well-known "lineæ albicantes." Œdema of the

[1] *Brit. Med. Jour.*, 1906, i, 1157.
[2] *Lancet*, 1913, i, 1309.
[3] *Compt. rend. Soc. biol.*, 1899, **51**, 674.
[4] *Deutsch. Arch. f. klin. Med.*, 1901, **71**, 79.

abdominal walls may obscure the signs of ascites. The costal margins are expanded, and the abdomen moves little on respiration.

On *palpation* the resistance is fairly uniform. The characteristic thrill is readily brought out by flicking the surface in one flank. When the hand is placed flat on the abdomen and the tips of the fingers are sharply flexed, fluid between the abdominal wall and the liver or spleen, if enlarged, or an abdominal tumor, may be displaced and the firm surface of the previously obscured organ is distinctly felt; this is spoken of as "dipping."

Percussion brings out a dull note over the fluid, which collects first in the pelvis and then passes upward into the loins and hypogastric region, producing a horseshoe-shaped area of dulness. The umbilical and epigastric regions remain resonant except in those cases of chronic peritonitis in which, from shortening of the mesentery, the intestines cannot reach the front of the abdomen. The characteristic horseshoe-shaped distribution of dulness is sometimes disturbed by flatulent distention of the large intestine, especially in the right iliac fossa; while, conversely, dulness in the flanks may be due to liquid feces and not to free fluid in the peritoneum. Light percussion gives a duller note than more forcible percussion, as pressure displaces a layer of fluid between the abdominal wall and an adjacent coil of distended intestine. A very important sign of free fluid in the abdominal cavity is *shifting dulness*. The presence of adhesions may interfere with this test, and for its success some of the intestines must contain gas. In cases in which the amount of fluid is not sufficient to give this sign the patient may be put in the knee-elbow position and the anterior surface of the abdomen then percussed in the most dependent position for an impaired note.

Results.—Distention of the abdomen gives rise to fulness, weight, and pain in the tense parietes; "pain is a very common symptom in ascites, but is seldom or never described in accounts of that condition" (Gee[1]). The abdominal viscera are embarrassed, so that dyspepsia and constipation are common, the latter being partly due to the flabby condition of the stretched abdominal muscles. The uterus may be displaced and fluctuation can be detected by the finger on pelvic examination. The abdominal muscles atrophy, and the recti separate so that a hernial protrusion may occur. Pressure on the inferior vena cava may induce œdema of the legs, while compression of the renal veins leads to chronic venous engorgement of the kidneys and scanty high-colored urine of increased specific gravity with sometimes a trace of albumin—resembling that of a failing heart. Albuminuria may, of course, be due to renal disease which is often associated with chronic peritonitis. The upward displacement of the diaphragm pushes the heart up, so that the apex beat may be in the third interspace; in some cases there is a soft, systolic apex murmur, which may disappear when the abdominal distention is relieved. The breathing may be embarrassed and cyanosis appear, the underlying condition being collapse and œdema of the lower lobes of the lungs. In rare cases the pulmonary engorgement is

[1] *Clinical Aphorisms from Dr. Gee's Wards, St. Bartholomew's Hospital Reports*, 1896, **32**, 44. Aphorism No. 128.

so extreme that there is hemoptysis. The percussion note at the bases of the lungs behind is impaired. From diminished resistance of the peritoneum infection with microörganisms of a low virulence may supervene, especially after paracentesis.

Diagnosis.—Differential Diagnosis.—The physical signs of free fluid in the abdominal cavity may, to a certain extent, be reproduced by large cysts occupying almost the whole of the abdominal cavity. In women confusion sometimes arises between a large ovarian or parovarian cyst and ascites. An ovarian cyst may have been first noticed in one position and subsequently spread upward into the abdomen; the maximum abdominal girth is below instead of above the umbilicus; the umbilicus may be displaced toward the thorax or to one side of the middle line, dulness is present in the middle line and not in the flanks, and there is little constitutional disturbance, the ill effects being almost entirely mechanical. Ovarian cysts, however, may be accompanied by ascites set up by chronic inflammation of the peritoneum covering them, or they may rupture. In rare instances a huge hepatic abscess, hydatid cyst, pancreatic cyst, or hydronephrosis has been regarded as ascites; but in these cases there may be a history of localization of the cyst at an earlier period, and even at a later stage the abdomen is hardly ever so fully occupied as to present all the physical signs of ascites. In encysted peritonitis the physical signs are those of a large cyst, and the dulness does not shift as it does in ascites.

Among solid or semisolid tumors the rare but remarkable fatty tumors may very closely simulate ascites and their true nature be only suspected after repeated fruitless tappings (see page 971).

Diffuse *colloid carcinoma* is rare, but, unless complicated by ascites, thrill and fluctuation are absent. In exceptional instances a distended urinary bladder, or even gall-bladder, has been regarded as ascites. As the patient should always pass water, or, if he cannot, be catheterized before the abdomen is tapped, the possible error of regarding a greatly dilated urinary bladder as ascites would be corrected. A greatly dilated stomach and a pregnant uterus with hydramnios have also been thought to be ascitic effusions. The absence of the concomitant signs of pregnancy should prevent ascites from being regarded as that condition; but a case of a uterine fibroid combined with ascites has been regarded as pregnancy. Great obesity may imitate ascites, and it may be very difficult to exclude the presence of, at any rate, some free fluid in the abdomen. The distention due to tympanites should not be mistaken for ascites, since the abdomen is everywhere resonant, but when the abdominal parietes are laden with fat the percussion note may thereby be much impaired. Occasionally in adults with chronic intestinal obstruction distention of the intestine with fluid may simulate ascites, and in children with chronic enteritis this condition of pseudo-ascites has led to laparotomy. In such cases succussion due to the presence of gas as well as fluid feces in the intestines can often be obtained. Conversely, the writer has seen a case of ascites with constipation and vomiting due to gastritis regarded as intestinal obstruction.

The Diagnosis of the Cause of Ascites.—Jaundice points to malignant disease or cirrhosis of the liver, being deep in malignant disease and comparatively slight in cirrhosis. Recurrent ascites usually indicates simple chronic peritonitis. The evidence of a growth elsewhere makes the diagnosis of malignant disease almost certain. Heart disease or tuberculosis elsewhere renders backward pressure or tuberculous peritonitis probable. A history or evidence of alcoholism points to cirrhosis. Thrombosis of the portal vein, which is often a complication of cirrhosis, can hardly be diagnosed, but melena and rapid onset of ascites may suggest it. A history or the manifestations of syphilis point to this form of liver affection; the Wassermann reaction may be more marked in the ascitic fluid than in the blood (Esmein and Parvu[1]).

Enlargement of the liver, if quite smooth, may point to lardaceous change; if rough, to cirrhosis; and if extreme or definitely nodular, to malignant disease. Less marked enlargement and irregularity may suggest syphilis of the liver, a conclusion which would be strengthened by other evidence of syphilis, and may be clinched by recovery under antisyphilitic treatment. If ascites be associated with general œdema and albuminuria, renal disease is the probable cause. Multiple palpable tumors in the abdomen point to malignant disease, or in a less degree to tuberculous peritonitis. Fever and concomitant pleurisy are in favor of tuberculosis, as are scars in the neck. But enlarged glands above the left clavicle point to malignant disease.

By laparoscopy or inspection of the peritoneal cavity by means of a fine cystoscope introduced through a trocar after the ascites has been evacuated and air introduced, Jacobæus[2] has been able to recognize the cause of the ascites.

Age has some bearing on the diagnosis. Ascites in stillborn children is generally due to congenital syphilis. Tuberculous peritonitis is the commonest cause of ascites in children and young women, and cirrhosis, simple chronic peritonitis, and malignant disease in adults over forty years of age. Examination of the fluid drawn off may be of practical value. If blood-stained at the first tapping, malignant disease should be suspected; microscopic examination may show pieces of malignant growth or fragments of ovarian papilloma. In malignant disease multinuclear endothelial cells and a large number of cells showing atypical mitoses may be found, but in many instances the ascites is mechanical and due to pressure exerted by the growth, and shows a predominance of endothelial cells, or of lymphocytes probably from chronic irritation. In other cases, again, there may be a considerable number of polymorphonuclear leukocytes, probably as the result of subacute inflammation; hence a diagnosis of malignant disease cannot always be made from examination of the cells in the effusion alone. Tenacious fluid may be due to rupture of an ovarian cystadenoma, and microscopic examination of the cells may confirm this.

Turbid fluid of a high specific gravity (1.020) points to inflammation. If the predominating cells are polymorphonuclear leukocytes there is

[1] *Compt. rend. Soc. biol.*, 1909, **62**, 159.
[2] *Trans. XVII Internat. Congress*, 1913, London (Sect. Med.).

subacute inflammation; but if the cells are mainly lymphocytes, tuberculous infection should be suspected and guinea-pigs should be inoculated with the fluid. It should be remembered that many cases of clear ascites are tuberculous in origin. The detection of tubercle bacilli in the feces has established the diagnosis in doubtful cases of ascites (Rosenberger[1]).

In hepatic cirrhosis the fluid is clear and shows a preponderance of endothelial cells. If complicated by infection, as may occur after tapping, there may be a large number of polymorphonuclear leukocytes. When tuberculous peritonitis supervenes the number of small lymphocytes will increase, but the lymphocyte count may be high in uncomplicated cirrhosis (Cabot[2]). A high percentage of endothelial cells excludes acute or subacute infections and tuberculosis.

Prognosis.—This depends in the first place on the cause. Thus, ascites in malignant disease leaves no room for hope of recovery, while that of tuberculous peritonitis is often followed by permanent cure. The ascites that recurs again and again in cases with secondary ovarian papillomas implanted on the peritoneum or in some cases of solid ovarian growths (Osler[3]) may be cured by removal of the primary growth.

When ascites supervenes in an emaciated subject of hepatic cirrhosis, the prognosis is bad, and tapping is not likely to be required more than twice before death closes the scene. The association of jaundice with ascites is rare except in malignant disease and hepatic cirrhosis, and is therefore a bad prognostic. In simple chronic peritonitis paracentesis may be necessary for a prolonged period; Rumpf's[4] patient was tapped 301 times in sixteen years, and cases in which the abdomen has been punctured more than a hundred times are not very rare. The results of hepatic cirrhosis, of cirrhosis complicated by chronic peritonitis, and of chronic peritonitis alone, may be arranged in this order from the point of view of the severity of the prognosis. Thus, in 31 cases of uncomplicated hepatic cirrhosis the average duration of life after the first appearance of ascites was 98.6 days; in 12 cases of cirrhosis complicated with chronic peritonitis, 288 days; and in 9 cases of uncomplicated chronic peritonitis, 624 days (Ramsbottom[5]). In milky ascites the prognosis is bad. In rare cases ascites spontaneously disappears, and great diminution has been noted during an attack of fever.

Treatment in the first instance should be directed to the underlying cause, if this be known and amenable to cure, for example, syphilis of the liver or heart disease. In simple chronic peritonitis and hepatic cirrhosis no known drug exerts any direct action on the morbid process. The palliative treatment consists in attempts to diminish the passage of fluid into the peritoneal cavity and to effect its removal. A restricted intake of fluids or a "dry diet" is usually very disappointing. The results of a salt-free diet are not very striking.

The means for the removal of fluid from the abdominal cavity are: (1) By paracentesis, (2) by diuretics, and (3) by purgatives.

[1] *Am. Jour. Med. Sci.*, 1907, **134**, 830.
[2] *Jour. Am. Med. Assn.*, Chicago, 1912, **59**, 2295.
[3] *Lancet*, 1907, i, 1409.
[4] *Deutsch. Arch. f. klin. Med.*, Leipsic, 1895, **55**, 272. (Festschrift zu F. A. von Zenker.)
[5] *Medical Chronicle*, Manchester, 1906, **45**, 7.

1. *Paracentesis abdominis* is indicated when the abdominal distention causes pain or vomiting, when upward displacement of the diaphragm gives rise to dyspnœa, or to collapse and œdema of the lung and when there is considerable diminution in the amount of urine. In cirrhosis, hematemesis or incipient delirium tremens indicates the advisability of tapping an ascitic abdomen.

The abdomen is most advantageously tapped below the umbilicus in the middle line. If from adherent omentum no fluid is withdrawn in this position, the trocar and cannula must be introduced elsewhere. It has been recommended that the middle point of a line drawn from the anterior superior spine of the ilium to the umbilicus should be chosen, and that in order to avoid wounding the cecum or liver the left side should be selected. In rare instances fatal hemorrhage has followed puncture in this position from a wound of the deep epigastric artery. This accident may be suspected if, on withdrawing the cannula, pure blood comes in spirts, and should be met by ligature of the vessel.

Before the abdomen is tapped the urinary bladder should be emptied, and the site of the puncture percussed and be found to be dull. The patient should lie on his back with the head slightly raised; the skin in the neighborhood of the intended puncture should be cleaned and rendered aseptic. If necessary, the skin may be anesthetized by ethyl chloride and cocaine injected under the skin at the site of puncture. A comparatively small cannula should be used, so as to remove the fluid slowly. Rapid removal of fluid may lead to faintness. The sterilized trocar and cannula should then be introduced, the trocar withdrawn, and the shield fixed in position by plaster. The fluid is then allowed to run away through a thin india-rubber tube. This takes some hours to drain away, and during this period the abdomen may be protected by a cradle, and a many-tailed bandage or a binder should be kept comfortably tight over the abdomen. If the flow stops before the abdomen has been fairly well evacuated, the india-rubber tube should be "milked," starting from the cannula. When the fluid has ceased to run, the cannula should be withdrawn and the small wound closed by a pad of absorbent cotton-wool soaked in collodion. The abdomen should be bandaged or tightly strapped to prevent rapid accumulation of the fluid and flatulent distention. In some instances good results have followed the injection through the cannula, after the abdomen has been nearly emptied, of a dram of adrenin chloride, 1 to 1000, in an ounce of water. It has been shown experimentally that injection of adrenin into the peritoneal cavity increases absorption of fluid (Fleischer and Loeb[1]). Apart from wounding a bloodvessel in the abdominal wall, there are very few dangers connected with paracentesis. In extremely rare instances acute pulmonary œdema has occurred. Wounding of the abdominal viscera should be avoided if proper care be taken. Repeated tapping may set up some degree of chronic peritonitis; acute peritonitis is, with ordinary attention to aseptic precautions, very rare. Prolonged or permanent drainage is not advisable.

[1] *Jour. Exper. Med.*, 1910, **12**, 288.

2. *Diuretics* are disappointing and their use should not be persisted in when there are indications that paracentesis is necessary. They sometimes succeed after paracentesis, probably because the kidneys are then in a better position to act; for a large ascitic effusion exerts pressure on the renal veins and this chronic venous engorgement is induced. Good results have been obtained by the intramuscular or intravenous injection, once or twice a week, of 1 to 2 cc. of 10 per cent. solution of novasurol, a double salt of sodium mercurichlorphenyl oxyacetate and barbital, containing 34 per cent. of mercury; it is given in conjunction with ammonium chloride and a salt-free diet (Rowntree, Keith and Barrier[1]). In heart cases Baillie's or Addison's pill, containing digitalis, squill, and mercury, is commonly used; citrate of caffeine, diuretin, or theocin combined with digitalis may also be given. In ascites due to other causes acetate, citrate, or tartrate of potash, and urea may be tried.

3. *Purgation.*—Moderate purgation by calomel or jalap and salts, such as tartrate of potassium or sulphate of magnesium and sodium combined, may be tried; but drastic purgatives, such as elaterium, should be avoided, as the patient's strength may be seriously impaired.

Operative treatment in tuberculous peritonitis and hepatic cirrhosis is considered elsewhere (pages 825, 968).

Hemoperitoneum.—The presence of pure blood free in the peritoneal cavity is somewhat rare, and must be distinguished from blood-stained ascitic effusions. The causes of intraperitoneal hemorrhage are: (1) Rupture of ectopic gestation; this is the most frequent cause; of 20 cases of intraperitoneal hemorrhage examined by Dudgeon and Sargent,[2] 17 were due to this cause. Rupture of an ovarian follicular cyst or of a lutein hematoma may cause extensive intraperitoneal hemorrhage; Phaneuf[3] has collected 22 such cases with ruptured follicular cysts and 20 with ruptured lutein cysts. (2) Traumatic rupture of the spleen, liver, or mesentery. (3) Rupture of aneurisms of the cœliac axis, or of the superior mesenteric, hepatic, or other intra-abdominal arteries. Aneurisms of the abdominal aorta usually rupture behind the peritoneum in the first instance, but may subsequently leak into the peritoneal cavity. (4) From leakage of a hemorrhagic or vascular new-growth, for example of the liver or adrenals. (5) From rupture of varicose or dilated veins; thus, most profuse hemorrhage may occur from rupture of a dilated vein on the surface of a subperitoneal fibromyoma. In 1921 Ernst and Gammettoft[4] collected 33 cases and critically accepted 23; trauma appears to be an important factor in causing the hemorrhage. Rupture of a varicose vein in the broad ligament is rapidly fatal, but is extremely rare. The writer has seen a large quantity of blood in the peritoneal cavity from traumatic rupture of a vein in peritoneal adhesions. (6) From rupture of a hemorrhage into the suprarenals. (7) In very rare instances repeated peritoneal hemorrhages may occur without any known cause.

[1] *Jour. Am. Med. Assn.*, 1925, **85**, 1187.
[2] *Lancet*, 1905, i, 474.
[3] *Jour. Am. Med. Assn.*, 1924, **83**, 658.
[4] *Acta Gyn. Scandinav.*, Upsala, 1921, **2**, 104.

In Cheeseman and Ely's[1] case the abdomen was tapped 43 times in five years and then spontaneous cure occurred. Both pleuræ had previously presented recurrent hemorrhagic effusions.

Intraperitoneal hemorrhage, although sterile at first, rapidly becomes infected. Of Dudgeon and Sargent's 20 cases, only one was completely sterile, and that was operated upon two hours after the onset; the organism isolated by these observers was a white staphylococcus. This explains (*a*) the fever which may follow intraperitoneal hemorrhage, and was formerly referred to the absorption of fibrin-ferment; and (*b*) the onset, if the patient survived sufficiently long, of peritonitis.

Symptoms.—Sudden pain which marks the extravasation of blood into the peritoneal cavity is followed by faintness, rapid and feeble pulse, restlessness, sighing respiration, vomiting, attacks of colicky pain, bloodlessness and extreme pallor, sweating, and collapse. In some cases, for example, rupture of an aneurism, death occurs at once. In other cases, especially when the blood is poured out less rapidly, the symptoms may imitate those due to perforation of a gastric ulcer.

Sequelæ.—If the patient is not operated upon and survives, acute general peritonitis will follow, unless, indeed, the extravasation be sufficiently localized to become encysted and form a peritoneal sanguineous cyst (see page 976).

Diagnosis.—With symptoms of internal hemorrhage and a history of recent and severe trauma the diagnosis is easy. On the other hand, ruptured ectopic gestation may so closely resemble acute perforative peritonitis that the condition is not suspected until the abdomen is opened. Cullen has drawn attention to a bluish discoloration of the navel in hemoperitoneum. When collapse occurs in a patient known to have an intra-abdominal tumor the occurrence of hemorrhage may be suspected.

Prognosis is best in ruptured ectopic gestations, but it is fatal in ruptured aneurisms and eventually in leaking malignant growths.

Treatment.—When the cause is a ruptured extra-uterine gestation or spleen the only course is removal of the ruptured organ.

Choleperitoneum.—Rupture of the bile passages with effusion of bile into the peritoneum usually sets up peritonitis, because the bile is commonly infected; but escape of aseptic bile into the peritoneal cavity need not cause inflammation; and in rare instances large bilious effusions result. This condition was named choleperitoneum by Dévé,[2] who in 1918[3] collected 69 cases due to rupture of a hydatid cyst which either before or after the rupture was in communication with a bile duct. The abdomen usually enlarges slowly, but it may do so rapidly. There is no fever, and jaundice does not occur, but the umbilicus may be yellow (Ransohoff[4]). The effusion is very apt to recur, and several tappings may be required. Kallmark[5] in recording a localized collection of bile (cholocele) under the diaphragm after biliary colic suggests rupture of intrahepatic bile ducts as the source of bile in cases without obvious rupture of the extrahepatic ducts.

[1] *Am. Jour. Med. Sci.*, 1899, **118**, 166.
[2] *Rev. de chir.*, Paris, 1902, **26**, 67.
[3] Ibid., 1918, **37**, 125.
[4] Quoted by Cullen: *Diseases of the Umbilicus*, p. 307.
[5] *Acta chir. Scandinav.*, 1924, **57**, 169.

ACUTE DIFFUSE PERITONITIS

Although acute peritonitis means acute inflammation of the peritoneum, the term is used to describe cases showing the clinical effects of acute infection of the peritoneum, namely, septicemia and toxemia, in which there may be very little or no manifest inflammatory reaction on the part of the peritoneum. These cases are more suitably described as "acute peritoneal infection." Thus, although it may sound paradoxical, the most severe cases of peritoneal infection often show the least evidence of inflammatory reaction. Acute diffuse peritonitis is not necessarily universal and coextensive with the whole area of the peritoneum. Strictly speaking, cases of acute peritonitis might be divided into (1) circumscribed, (2) diffuse or spreading, and (3) universal or total. But in practice acute peritonitis is usually considered as either (1) circumscribed or localized, or (2) spreading, general or diffuse. There is some unavoidable vagueness about the terms general and diffuse as descriptive of the extent of the peritonitis seen at an operation; thus the words employed may be meant to imply universal infection and inflammation of the peritoneum throughout the whole of the abdomen, or only that at the time of the operation the peritonitis was not strictly localized. It has, therefore, been suggested that the term universal should be employed instead of general, and progressive instead of diffuse. The term diffuse will be employed here.

Pathogeny.—Although chemical poisons, such as turpentine, croton oil, and nitrate of silver, when introduced into the peritoneal cavity of animals can set up acute inflammation, it is safe to assume that in practice all cases of acute peritonitis in man are due to infection.

The mere entry of microörganisms into the peritoneal cavity is not alone enough to produce peritonitis. The defensive powers of the peritoneum, viz., the phagocytic action of the endothelial and other cells, the bactericidal power of the peritoneal fluid depending on the presence of antibodies, and absorption—which destroy and remove the invading bacteria—are able to prevent the production of inflammation. With regard to absorption from the peritoneal cavity, it should be explained that, while the removal of bacteria in comparatively small quantities and their destruction in the lymphatic glands and other organs prevent the onset of peritonitis and are therefore beneficial, the passage of large numbers of virulent bacteria into the general circulation gives rise to a grave and often fatal bacteriemia. Death from "shock" after perforation may in all probability be explained in this way. The absorptive powers of the peritoneum also militate against peritonitis by removing fluid in which microörganisms might multiply. The defensive powers of the peritoneum were divided by Andrewes[1] into those which are physiological, or the "first line of defense," and those which come into play when inflammation is set up, or the "second line of defense." These two lines of defense merge into each other in phago-

[1] *General Pathology and Bacteriology of Acute Peritonitis. System of Medicine* (Allbutt and Rolleston), 1907, **3**, 897.

cytosis, but the formation of fibrinous adhesions which localize the infective focus is a frankly inflammatory process.

When the defensive powers of the peritoneum are inhibited or prevented from exerting their full effects, bacterial invasion is enabled to set up peritonitis. Factors which reduce the resistance of the peritoneum, such as the sudden entrance of poisonous fluids, drying or trauma during the course of an operation, and possibly cold, may interfere with the absorptive and bactericidal powers of the peritoneum. The presence of solid bodies, such as particles of food, feces, blood-clot, concretions, or foreign bodies, or of ascitic fluid, may protect the bacteria, provide a nidus for their multiplication, inhibit absorption, and so enable them to produce their toxins and set up inflammation of the peritoneum.

Etiology.—Acute diffuse peritonitis may be (1) primary or (2) secondary.

1. The term *primary idiopathic peritonitis* has been employed in two senses. Formerly it was used to imply that inflammation attacked the peritoneum alone, the rest of the body being healthy, and that its cause and origin were unknown. Peritonitis formerly thought to be due to rheumatism or to cold comes under this head. Since it has been recognized that acute peritonitis is practically always infective, the term primary peritonitis was applied by Flexner[1] to cases in which, as there is no local focus in the abdomen to account for the infection of the peritoneum, it is assumed that microörganisms have reached the peritoneum by the blood- or lymph-stream. Hematogenous peritonitis occurs as a terminal infection in chronic nephritis, arteriosclerosis, cancer, and other conditions which reduce the bactericidal power of the blood. Some cases of peritonitis complicating erysipelas, epidemic streptococcic sore throat, or other infections, and about one-half of the instances of pneumococcic peritonitis, would also appear to be primary and so of hematogenous origin. Peritonitis in scarlet fever is rare; it may be primary or secondary. Plateau[2] collected 12 cases, 8 of which showed streptococcic infection. Among Zierold's[3] 28 cases of primary peritonitis 1 only was pneumococcic; like Rabinowitz[4] he emphasized the streptococcic and pharyngeal origin, the infecting organism being *Streptococcus hemolyticus*. Since a minute local focus, such as a microscopic abscess in the appendix, may be easily overlooked, a most exhaustive postmortem examination is necessary before a case of primary idiopathic peritonitis can be accepted. Probably about 10 per cent. of the fatal cases of general peritonitis are of this nature. It occurred in 12 out of 106 cases examined by Flexner and in 9 out of 105 cases at the Massachusetts General Hospital (Manahan[5]). The infection is usually single; thus out of Flexner's 12 cases no bacteria were found in 2, in 9 there was a single infection, and in 1 a mixed infection.

2. *Secondary peritonitis*, in which infection is due to some local lesion either in or in the immediate neighborhood of the abdomen, accounts for the great majority of cases of acute diffuse peritonitis.

[1] *Philadelphia Med. Jour.*, 1902, **2**, 1019.
[2] *Arch. Pediat.*, 1924, **41**, 535.
[3] *Ann. Surg.*, 1924, **79**, 418.
[4] *Am. Jour. Med. Sci*, 1919, **157**, 797.
[5] *Boston Med. and Surg. Jour.*, 1905, **162**, 345.

(*a*) Wound or operation introducing infection into the peritoneal cavity, *e. g.*, after herniotomy. To this group Flexner applied the term exogenous. But it must, of course, be remembered that postoperative peritonitis may be due to bacterial infection derived from the viscera.

(*b*) Due to infection derived from the abdominal viscera. This may depend on gross perforation of their walls or be due to inflammation allowing microörganisms to pass through the intestinal walls. This is Flexner's endogenous group. It will be convenient to mention the affections of the abdominal viscera which may cause acute peritonitis.

Stomach.—Perforation of a gastric ulcer; perforation due to rapidly growing, soft, and necrosing carcinoma; acute suppurative (or phlegmonous) gastritis; acute gastritis due to corrosive poisons.

Small Intestines.—Traumatic rupture, perforation by sharp foreign bodies; perforating ulcers, duodenal; jejunal peptic ulcer, occurring in cases of gastrojejunostomy, especially, it is said, after the anterior operation; typhoid ulcer (peritonitis in rare instances occurs without any gross perforation); uremic ulcer; acute enteritis; strangulation, kinking, volvulus, intussusception; internal hernia; infarction.

Appendix.—Perforation as a result of acute infective inflammation; from rupture of an abscess in the walls of the appendix or in its neighborhood, or from acute appendicitis.

Colon.—Perforation, traumatic or by a foreign body from within. Perforating ulcer, stercoral or dysenteric; in connection with carcinoma, either from rupture of a distention ulcer or leakage through necrosing growth. Extremely acute inflammation, in strangulation, volvulus, intussusception. Wounds, perforation of the rectum by a bougie, or by the nozzle of an enema syringe.

Gall-bladder.—Acute, phlegmonous, or gangrenous cholecystitis. Rupture of an inflamed gall-bladder.

Liver.—Rupture or leakage of an abscess or of a suppurating hydatid cyst. Abscess may be multiple and due to arterial infection, suppurative pylephlebitis or cholangitis. In new-born infants phlebitis of the umbilical vein gives rise to peritonitis.

Spleen.—Rupture of an abscess, or of a suppurating infarct.

Mesenteric Glands.—Rupture of a suppurating lymphatic gland into the general cavity of the peritoneum.

Ulceration and perforation of the *urinary bladder* or of sacculi in connection with it.

Suppurating and gangrenous ovarian cysts.

Pyosalpinx and infection spreading from the Fallopian tubes. Riedel[1] has shown reasons for believing that salpingitis is a more important cause of general peritonitis under ten years of age than in adults.

Perforation of the uterus by a sound.

Rupture of an abscess into the peritoneal cavity, especially of a periappendicular abscess; this may follow rough manipulation. It is remarkable how rarely erysipelas or suppuration in the abdominal parietes gives rise to peritonitis; this probably depends on the lymphatics being

[1] *Arch. f. klin. Chir.*, 1906, 81, 186.

independent. Although peritonitis may lead to infection of the pleuræ, an empyema hardly ever ruptures into the abdominal cavity. Inflammation readily spreads from the pancreas to the peritoneum of the lesser sac. Retroperitoneal suppuration, such as that due to tuberculous ostitis of the spine or to renal calculi seldom infects the peritoneum.

As giving the relative importance of the various starting-points of acute peritonitis, Benda's[1] 446 cases of acute diffuse peritonitis examined after death may be referred to. The vermiform appendix was the starting-point in 115 cases, the stomach and duodenum in 68, the rest of the intestine in 118, the female genitals in 81, the gall-bladder in 10, the kidney and urinary bladder in 10, the pancreas in 2, the spleen in 1; 35 were unknown, 4 were postoperative, and 2 hematogenous.

The *sex* and *age* incidence depend on those of the commonest causes of peritonitis, perforating gastric ulcer and pelvic infections being the most frequent etiological factors in women, and appendicitis in children and young males. In 200 fatal cases at St. George's Hospital there were 107 males and 93 females; the average age of the 200 cases was thirty-two years, being 34.26 in the males and 29.3 years in the females. In infants acute peritonitis is usually due to infection from the umbilicus.

Bacteriology. A large number of microörganisms have been found in human peritonitis. In many instances there is a mixed infection, and difficulty arises in apportioning the share that the organisms present have taken in producing peritonitis. The organisms found in peritonitis are in nearly all instances morphologically the same as those commonly present in the healthy intestine.

Bacillus coli is very commonly found, and considerable discussion has taken place whether its importance is commensurate with its frequency. It has been regarded as the all-important factor in peritonitis and, on the other hand, it has been thought that the *B. coli*, being more hardy than other bacteria, may overgrow them and so be found postmortem to the exclusion of other microörganisms which are the real factors in producing peritonitis. It is naturally found most often in cases of peritonitis due to infection from the alimentary canal, and is very frequently present in association with some other organism. In 56 cases of peritonitis due to bowel infection, Flexner found the *Bacillus coli* in 43, in pure culture in 8, and in association with other organisms in 35. Dudgeon and Sargent,[2] as the result of bacteriological examination of 270 cases, came to the conclusion that the colon bacillus is the most important factor, and that it is found in the largest number of fatal cases. Its virulence varies greatly, and while less dangerous than the streptococci and *Bacillus pyocyaneus*, it is more frequently present. With mixed cultures a very virulent peritonitis is set up.

A white *staphylococcus*, which is not the same as the *Staphylococcus pyogenes albus* described by Rosenbach, and has often been regarded as due to contamination from the skin, and is probably Welch's *Staphylococcus epidermidis albus*, has been found by Dudgeon and Sargent to

[1] Quoted in *A System of Surgery*, von Bergmann, von Bruns, and von Mikulicz, translation, vol. **4**, p. 165.

[2] *The Bacteriology of Peritonitis*, Constable & Co., London, 1905.

be the first organism to appear in the peritoneal cavity in cases of early peritonitis, and to pass through the walls of the inflamed intestine before more virulent organisms. They found it in 108 out of 258 peritoneal lesions.[1] It gives rise to an exudation rich in phagocytes, and thus exerts a protective action against more virulent microörganisms.

Streptococci are found in a considerable percentage of the cases. Flexner found them second in order of frequency both in his primary and secondary groups of peritonitis. As streptococci are among the normal saprophytes of the intestinal canal, it is natural that they should be commonly present in cases of peritonitis due to intestinal lesions; but the *Streptococcus pyogenes* has not been found normally in the alimentary canal, and streptococci found in the peritoneum are not necessarily *Streptococcus pyogenes*, and may be the saprophytes of the intestine. Peritonitis due to *Streptococcus pyogenes* is the most severe and fatal form; there is little or no local reaction, the phagocytes being powerless against the virulent microörganisms which are rapidly absorbed into the circulation and give rise to fatal bacteriemia in twenty-four to forty-eight hours from liberation of their endotoxins.

Staphylococcus pyogenes aureus was found by Flexner in 15 out of 34 cases of exogenous peritonitis, being in pure culture in 12 and mixed in 3. It was present in 3 only in 39 cases of endogenous peritonitis. It gives rise to a virulent form of peritonitis.

Bacillus pyocyaneus is responsible for a certain number of cases of acute peritonitis, and ranks next to the *Streptococcus pyogenes* in its virulence. It does not produce green pus in the peritoneal cavity, as it often does in a local abscess. Dudgeon and Sargent have shown that *Bacillus coli* will not grow in the presence of *B. pyocyaneus*.

Bacillus typhosus has been found in a few cases of peritonitis due to perforation of typhoid ulcers, and even after rupture of the spleen. But it is combined with saprophytic organisms, and it is doubtful what importance should be attached to its presence.

Other organisms such as *Bacillus lactis aërogenes* (Churchman[2]), *B. influenzæ* (Hull and Fisch[3]), *B. proteus*, *B. anthracis*, are occasionally found. With regard to anaërobic organisms, there has been a good deal of discussion; Veillon and Zuber and Tavel and Lanz conclude that anaërobic organisms are of importance in the production of appendicitis and peritonitis, while Dudgeon and Sargent employed strictly anaërobic precautions in a number of cases of appendicitis and in other varieties of peritonitis, but failed to find anaërobic organisms except in one case of gangrenous appendicitis with abscess in which *Bacillus aërogenes capsulatus* was found in addition to *B. coli* and a streptococcus. As the result of the presence of anaërobic organisms the peritonitic exudate may become putrid.

Morbid Anatomy.—The appearances necessarily vary with the causes and stages of acute peritonitis. In the most rapidly fatal cases, there may be little or no morbid change. In other cases the earliest visible

[1] *Lancet*, 1906, ii, 1337.
[2] *Johns Hopkins Hosp. Bull.*, 1911, **22**, 116.
[3] *St. Louis, Med. Rev.*, 1903, **48**, 55.

change is congestion of the small bloodvessels of the peritoneum; this is not uniformly distributed, but is naturally best marked and at first confined to the starting-point of the inflammation and to the omentum which is often adherent to the focus of infection. Further, it is more marked on the visceral than on the parietal peritoneum, and is in most instances not diffuse, but is confined to longitudinal lines which correspond with the spaces left between contiguous and distended coils of intestine. The next change is the exudation; at first there is slight dulling of the smooth peritoneal surface, which appears finely granular, and on scraping yields a little fibrin. This fibrin is sticky and as it increases in amount glues the intestines together and collects in the triangular chinks left between adjacent coils. At first the fibrin is thin and clear, but it becomes opaque, and may be yellow or even of a green tint. Large masses of fibrin may eventually form and show a somewhat spongy or reticulated structure.

The fluid portion of the exudation, usually comparatively small, may in some instances be considerable (several quarts). It collects between the intestinal coils; during life it is often mainly in the loins, but after death it is more commonly seen in the pelvis. Its characters vary much in different cases: it may be (1) serous; (2) serofibrinous, turbid, with pieces of fibrin floating in it, and of a specific gravity of 1.018 or upward; (3) fibrinous; (4) fibrinopurulent; (5) purulent; (6) sanious; (7) putrid, due to the presence of putrefactive anaërobic organisms. In such cases there may be free gas in the peritoneal cavity without any perforation of the hollow viscera. In virulent streptococcic infection there is a little thin, odorless fluid; in gonococcic infection there is a dry, fibrinous exudate with hardly any pus or serum; in pneumococcic peritonitis the exudate resembles that in a pneumococcic empyema, and in *Bacillus coli* infections there is a thick, creamy pus. In some instances of peritonitis secondary to cholecystitis the exudation may be bilious without any gross perforation of the biliary tract.

The *progressive fibrinopurulent form of peritonitis* described by Mikulicz is transitional between circumscribed and diffuse peritonitis. There is a gradually extending area of foci of pus enclosed in fibrinous adhesions and in rare instances the whole of the peritoneal cavity may be involved. Rupture of an encysted collection of pus may cause purulent peritonitis.

The intestines are in a state of paralytic distention, the walls somewhat swollen, œdematous, and softened from inflammation so that the peritoneum readily strips off and the intestine may rupture if pulled upon. In children there may be retrograde intussusceptions produced during the death agony. The peritoneum may show scattered small hemorrhages, and small extravasations of blood are not uncommon in the ovaries. The omentum is often adherent to the starting-point of the peritoneal infection, *e. g.*, the appendix. The formation of adhesions depends on shedding of the endothelium for as long as it remains intact no adhesion occurs (Cunningham).[1]

The lymphatics become filled with exudations and cells, and infection

[1] *Johns Hopkins Hosp. Bull.*, 1924, 35, 111.

is conveyed to the lymphatic glands in the anterior mediastinum; these glands are swollen, reddened, and contain microbes. As the result of toxic absorption the solid viscera, such as the liver, pancreas, spleen, kidney, show cloudy swelling of their cells and areas of focal necrosis. Rarely other serous membranes, especially the pleuræ, are inflamed as the result of a concomitant infection—an acute polyorrhomenitis. In prolonged cases, especially in pneumococcic and puerperal peritonitis, local abscesses may form. These if left alone may perforate in various directions, into hollow viscera, or even externally at the umbilicus.

Microscopically the endothelium of the peritoneum, especially of the omentum, early shows proliferative changes; the cells enlarge; their nuclei become swollen and divide by direct and then by indirect nuclear division. The cells ("macrophages" of Metchnikoff) thus produced vary in size, but some are indistinguishable from lymphocytes. The surface of the endothelial cells is covered by a layer of fibrin containing leukocytes, and there is small round-celled infiltration of the subendothelial tissues. Coarsely granular eosinophilic cells constitute a considerable proportion of the immense number of leukocytes attracted to the bloodvessels of the part; this local accumulation is correlated with the diminution of eosinophilic cells in the peripheral circulation (Opie[1]). At a later stage the cell infiltration of the underlying structures becomes more intense and extensive, and the peritoneal endothelium is destroyed. If the inflammatory process be short-lived the endothelium survives and the fibrin is eventually absorbed, so that the formation of adhesions is prevented. If the inflammatory process be continued the endothelial cells are destroyed and adhesions form.

The exudation and fibrin present on the surface of the peritoneum are protective by (*a*) enabling phagocytosis and bacteriolysis to take place, (*b*) by blocking up the lymph channels and so preventing absorption from the peritoneal cavity, and (*c*) by preventing the passage of microörganisms from the lumen through the walls of the inflamed intestine.

Cytology.—As the result of experimental bacterial infection, Durham found a leukopenic stage lasting an hour, the normal hyaline and eosinophilic cells disappearing from the peritoneal fluid, which becomes increased in amount, while the lymphocytes remain. The disappearance of the cells is due to their being collected into balls on the surface of the peritoneum, especially on the omentum. In very virulent infections the leukopenic stage may persist until death. According to Dudgeon and Ross's[2] experiments the first cells found in the exudation are either small lymphocytes or coarsely granular eosinophiles; subsequently there are polymorphonuclear leukocytes (Metchnikoff's "microphages," microxycytes) which are derived from the blood; these cells have been found by Beattie[3] to diminish in number in non-fatal cases in from forty-eight to sixty hours after the onset, but to persist until death in fatal cases. They are active phagocytes, as are also the mononuclear cells (macrophages) derived from the endothelial cells of the peritoneum, which, however, according to Buxton,[4] are unable to digest bacteria

[1] *Trans. Assn. Am. Phys.*, 1904, **19**, 136.
[2] *Brit. Med. Jour.*, 1905, ii, 1043.
[3] *Jour. Path. and Bacteriol.*, Edinburgh and London, 1903, **8**, 129.
[4] *Brit. Med. Jour.*, 1907, ii, 1422.

effectively in the absence of an early and marked polymorphonuclear reaction. Dudgeon and Ross state that the coarsely granular eosinophilic leukocytes (megoxycytes), which are usually regarded as non-phagocytic, are, in the early stages of peritoneal infection, among the important if not the most important phagocytes.

The peritoneal exudation is not infrequently free from microörganisms and from phagocytes containing bacteria, while the surface of the intestine and the omentum shows their presence. This observation is important in the consideration of the question of "chemical" peritonitis, for it is clear that the peritoneal exudate may be sterile, and so suggest a non-bacterial peritonitis. The wall of the intestine shows small-celled infiltration around the vessels and fibrinous and serous exudation; the nerve cells of Meissner's, Auerbach's and the solar plexuses show degeneration (Laignel-Lavastine[1]).

After-results.—Acute peritonitis leaves behind it some slight thickening and opacity of the peritoneum; in cases in which blood has been extravasated pigmentation may be due to altered blood-pigment. As the result of organization of fibrin, adhesions are commonly seen, but it is remarkable how completely they may disappear in course of time.

Symptoms.—The signs and symptoms of diffuse peritonitis vary quite widely in different cases; this depends on the cause of the peritonitis and on the virulence of the infecting organisms. It will, therefore, be best to give a very brief description of a common form of peritonitis, then to detail the manifestations that may occur in the various forms of peritonitis, and lastly to refer to special forms, pneumococcic, gonococcic, and puerperal.

The course of diffuse acute peritonitis can be most satisfactorily sketched by a short account of an ordinary case of perforative peritonitis. There is a sudden onset with agonizing burning pain and a feeling that something has given away; this is rapidly followed by collapse. These symptoms are due to the perforation. The abdomen is rigidly contracted and extremely tender. Tympanitic distention from escape of large quantities of gas into the peritoneal cavity is very rare at this stage. There is widespread and very severe pain which is exaggerated by any movement, so that respiration is costal and shallow, and there is frequent vomiting. The collapse passes off in a few hours, and for a time the patient appears fallaciously better; this period of latency or "stage of repose" (Symonds[2]) may be prolonged by the administration of opium or morphine. But when the disease is allowed to run its natural course, symptoms reappear and those of peritoneal inflammation become unmistakable; the abdomen gradually becomes distended, the legs being drawn up to relax the abdominal parietes, the arms usually lying above the head. There is extremely severe and constant pain, which becomes exaggerated in paroxysms and is made worse by the slightest movement, such as micturition; vomiting is frequent; the tongue becomes dry, the mouth parched, there is constant thirst, the temperature is somewhat raised, the pulse of high tension, wiry

[1] *Arch. de méd. et d'anat. path.*, 1905, **17**, 54.
[2] *Brit. Med. Jour.*, 1899, i, 520.

and rapid, the face pinched, anxious, and generally pale, and the aspect that of grave toxemia and of progressive exhaustion. As time goes on the abdominal distention increases, the pulse becomes thready, more rapid, and weaker, the skin is cold and clammy, and the extremities icy and blue, although the internal temperature may be considerably raised. Restlessness and anxiety persist, there is little or no sleep, the mind is usually clear to the end, but occasionally there is wandering or delirium. Pain, tenderness, and vomiting occasionally pass off shortly before death, which may be sudden from cardiac failure, but sometimes there is profuse vomiting just before death, and aspiration of the foul fluid into the lungs may be the last straw.

The Clinical Picture.—The underlying factors which are responsible for the clinical manifestations are: (1) Acute inflammation involving an extensive area. (2) Paralysis of the muscular walls of the intestines. (3) Septicemia and toxemia, due to the absorption first of microörganisms and toxins from the peritoneal surfaces and later of toxins from the paralyzed intestines. (4) Abstraction of water from the tissues.

The *onset* varies with the cause. When this is perforation of a hollow viscus, as in gastric or duodenal ulcer, the moment of the accident can usually be absolutely fixed. In typhoid fever, however, perforation may not be marked by sudden and acute pain, and from dulling of the patient's powers of perception the existence of acute peritonitis may be an anxious problem. In the late stage of renal disease, intra-abdominal new growths, cirrhosis, pulmonary tuberculosis, etc., the onset and even the existence of peritonitis may be latent and not suspected during life. In some cases, especially after abdominal operations and in intestinal obstruction, the onset of peritonitis is so gradual that it cannot be definitely fixed. In puerperal and occasionally in slowly progressive forms of peritonitis, such as may occur in connection with appendicitis, the development is gradual and insidious. With an acute onset there is more or less shock due to the damage done to the peritoneum by the sudden entry of the contents of an abscess or of a hollow viscus into the abdominal cavity. This shock may prove fatal before peritonitis has had time to develop.

The *facial aspect* of advanced peritonitis is characteristic, and has been described as "a composite photograph of hemorrhage, pain, and infection" (Crile). The face is pinched, the skin being tightly drawn over the bones, the eyes sunken and surrounded by dark rings, the skin gray or somewhat livid from failure of the circulation, and the expression anxious. This is the abdominal or Hippocratic face. In early stages, however, there may be nothing characteristic in the face, and the cheeks may be flushed.

The tongue, at first furred and moist, subsequently, from the loss of fluid and absence of saliva, becomes shrivelled, dry, and stained by the vomit. Unless the mouth is carefully and constantly cleaned, sordes collect. There is loss of appetite, and extreme thirst.

Position.—The patient lies on his back, the shoulders raised, and the thighs flexed so as to relax the abdominal walls as far as possible. The arms and head are tossed about and manifest the mental restlessness, but the rest of the body is kept as still as possible.

Pain is practically a constant symptom. It is only in cases in which a terminal peritonitis supervenes in the course of a chronic exhausting disease, such as gastric carcinoma or renal disease, or of an acute disease, such as typhoid fever, in which the mental faculties are greatly dulled, that pain is absent. The pain may be continuous with that of the causal perforation; in other forms of peritonitis it comes on more gradually, and steadily increases until it becomes intolerable. It is constant, but becomes worse from time to time, the exacerbations probably depending on movements of the intestines; vomiting, cough, or any kind of movement aggravates the pain, and accordingly the patient keeps the abdomen and trunk absolutely still, and holds the arms above the head, while the movements of the diaphragm are greatly restricted.

The pain is general all over the abdomen, but may be more marked in some one part, such as the umbilicus or the right iliac fossa, and may thus correspond with the starting-point of the disease. But this may be fallacious; for example, the pain may be most marked in the appendix region in perforated duodenal ulcer, and in pelvic appendicitis the pain is not uncommonly referred to the umbilicus. Toward the end the pain may disappear; this may be in part the result of the effusion and of intestinal paralysis, which prevent the intestines from rubbing against the parietal peritoneum; in part to the continued effect of toxemia on the exhausted sensorium. The diminution or disappearance of pain, therefore, does not mean that there is any improvement.

Tenderness.—Opinions differ as to cutaneous hyperesthesia. In order to test accurately for it, the skin, without any of the underlying tissues, should be carefully picked up between the finger and thumb. Head[1] states emphatically that it is absent, and Sherren[2] has never found it in general peritonitis due to appendicitis. Hale White,[3] however, says that it is often present, and H. Robinson[4] who found it in some cases suggests that it is only when the parietal peritoneum becomes inflamed that it appears. In acute peritonitis the abdominal reflexes are not exaggerated, as they would be if the tenderness were cutaneous (Head). Tenderness of the deeper tissues is due to implication of the parietal peritoneum and its somatic nerve supply in the inflammatory process. The tenderness gets progressively worse, and may be so extreme that the patient cannot bear the weight of the bedclothes; it is universal and corresponds with the extent of the peritoneum, being elicited by rectal and vaginal examination. Rectal examination may show ballooning of the rectum.

Rigidity of the Abdominal Walls.—In the early stages the muscles are firmly contracted from spasm, and there may even be retraction; this is most marked in perforative peritonitis. In strong and muscular men the rigidity is prominent and lasts for a considerable time; in fact, in very acute cases it may persist until the end. In women with very flaccid abdominal parietes there may be no appreciable rigidity. Although this muscular defense is one of the most common events in the course of

[1] *Brain*, 1893, **16**, 94.
[2] *Lancet*, 1903, ii, 816.
[3] *Manual of Medicine* (Allchin), 1903, **5**, 490.
[4] *Quart. Jour. Med.*, 1907–1908, **2**, 406.

acute peritonitis, it may be absent throughout; this is seen in gonococcic peritonitis, and even in cases in which there is no special atrophy of the abdominal muscles. This absence of rigidity is more likely to occur in non-perforative cases and in the somewhat slowly progressive fibrinopurulent peritonitis. As a result of this muscular spasm, the abdomen becomes more or less immovable; this is a valuable sign of peritonitis, but movement of the abdomen does not prove that peritonitis is absent. Muscular rigidity passes off when the patient is anesthetized.

Tympanites.—Except in the fulminating and rapidly fatal cases, the early rigidity gradually passes off, and in about forty-eight hours is succeeded by abdominal distention; in less acute cases this may be delayed for a day or two longer. The abdominal distention may come on more rapidly after rupture of the stomach and escape of gas into the abdominal cavity. The tympanites or meteorism of peritonitis is due to distention of the paralyzed intestines with flatus; to a slight degree accumulation of liquid feces in the dilated intestines, and inflammatory peritoneal exudate contribute to it. The abdomen becomes prominent, hyperresonant, and the skin tight, stretched, and shiny. Abdominal movement is abolished.

The distention pushes up the liver in such a manner that the normal relation of that organ to the parietes is altered, and very little of it remains in contact with the body wall; in extreme instances the thin edge of the liver looks upward and backward instead of downward and forward. In consequence, the hepatic dulness is diminished or obliterated, and this without any free gas in the abdominal cavity. Absence of liver dulness must not be taken as evidence of perforative peritonitis. The diaphragm is pressed up, so that the lower lobes of the lungs become œdematous and partially collapsed, and the breathing thus further embarrassed. The apex of the heart may be displaced upward.

The intestinal paralysis is probably nervous and due to reflex shock; it may be increased by œdema and inflammation of the muscular walls and the local action of toxins on the neuromuscular apparatus of the intestinal wall. But from the rapid onset of distention in some cases of peritonitis, before inflammation can have spread sufficiently into the intestinal wall to produce muscular paralysis, this is certainly not the only factor concerned. Distention is lessened by copious vomiting. The distention may force a coil of intestine into a hernial sac, and so suggest that the symptoms are due to strangulation of the bowel, but examination will show that the hernia is reducible.

Percussion is painful; when there is distention the note is usually tympanitic, but certain areas, especially the flanks, may be dull due to collections of peritoneal exudate or to the intestine being full of fluid. In rare instances a friction-rub can be heard. On the other hand, a valuable sign of intestinal paralysis is the entire absence of any gurgling sound when the abdomen is auscultated for five minutes at a time (Greig Smith).

Œdema of the abdominal wall is extremely rare; when it does occur it is usually in connection with a localized collection of pus, for example, appendicular abscess. It is not a sign of diffuse peritonitis.

Vomiting is one of the most characteristic and, next to pain, the most constant manifestations. It may be absent, however, especially in young children. In the early stages, of which it is often the first symptom, it is probably a reflex result of irritation of the peritoneum, although it has been regarded as due to the action of toxins on the medulla. In the later stages it is, like the vomiting of acute obstruction, due to a reflux flow of fluid into the stomach from the paralyzed intestines. That it depends on paralysis of the intestines and overflow into the stomach of their stagnating contents is supported by the rule that it is less prominent or absent in cases in which the bowels act or in which there is diarrhœa, as in puerperal peritonitis; further, washing out the stomach prevents the vomiting. It is commonly excited by taking fluid to relieve the urgent thirst. Handley[1] pointed out the frequency of paralysis of the intestine in two situations ("ileus duplex"), the pelvic colon becoming secondarily paralyzed from pelvic peritonitis due to extension from a focus elsewhere, such as appendicitis.

The vomited materials are first those of the stomach, then those of the upper part of the small intestine containing easily recognizable bile, and lastly feculent or stercoraceous matter of an extremely offensive character. In severe cases the vomit is often brown or dark in color from the presence of blood. The fluid is brought up with comparatively little effort, welling up into the mouth. The amount varies somewhat, but is much less than in mechanical obstruction. It is rather remarkable that vomiting occurs in cases of perforation of the stomach. The movement entailed in vomiting exaggerates the abdominal pain. Nausea is common, there is a bad taste in the mouth, and foul gas may be belched up. In the later stages retching may be substituted for vomiting.

Hiccough, when it occurs, usually comes on in the late stages of peritonitis when the abdomen is considerably distended. It is a reflex phenomenon, due to implication of the phrenic nerve.

Rigors are not common; they are seen in some cases of puerperal peritonitis, and in the prolonged form of progressive fibrinopurulent peritonitis.

Constipation is the rule, and, from intestinal paralysis, is often so marked, both for flatus as well as for feces, as to give the case the aspect of acute mechanical obstruction. An enema will, however, usually bring away some fecal matter in acute peritonitis without any improvement in the patient's condition; this does not hold good for mechanical obstruction. So constant is constipation in acute peritonitis that cases in which it is absent or in which the bowels can be made to act may generally be regarded as hopeful. In puerperal peritonitis, however, diarrhœa, due presumably to some peculiar form of toxin, is the rule. In other forms, except pneumococcic infection, it is exceptional.

Respiration.—As diaphragmatic and abdominal movements are greatly reduced or abolished, the respiratory excursions mainly depend on the intercostal muscles. The upper parts of the lungs are therefore employed to a larger extent as a means of compensation for the impaired

[1] *Brit. Jour. Surg.*, 1925, **12**, 417.

movements of the lower lobes, and some of the extraordinary muscles of inspiration come into action. The respirations are painful, shallow, and considerably increased in rate (40 to 50 per minute); coughing and deep breaths are restrained.

The *pulse* varies in character at different stages of the disease. It is nearly always regular, quickened, and becomes progressively more rapid, being 100 to 120 in the early stages, and becoming running or uncountable toward the end. In some instances the pulse may be little if at all accelerated, although there is extensive purulent peritonitis; this has been ascribed to interference with toxic absorption from blocking of the stomata and lymphatics, but is not necessarily a sign that the patient is improving. There is no correspondence between the rate of the pulse and the temperature; the temperature may be low and the pulse extremely rapid. Crile,[1] who found the average blood-pressure in 20 cases to be 166 mm. Hg., ascribes the small volume to the accumulation of blood in the splanchnic area and the hardness to reflex stimulation of the vasomotor centres from the peritoneum. The failure of the circulation is not due to the heart or to the vasomotor centre inducing paralysis of the bloodvessels in the splanchnic area, as was thought in the past. Both experimentally (Olivecrona[2]) and clinically (von Lichtenberg) it has been shown that the blood-pressure remains fairly within the limits of the normal until just before death, the fall then being ascribed to anemia of the vasomotor centre (Holzbach[3]). Absorption of toxins derived from protein decomposition causes dilatation and increased permeability of the capillaries with stasis and increased filtration through the damaged capillary walls, thus causing a diminished volume of blood, which is the important factor in the circulatory failure of peritonitis (Olivecrona).

The *temperature* is so extremely variable as to be of little or no value in diagnosis or as to the degree and gravity of the peritonitis. There is usually a more considerable difference between the rectal and the surface temperatures, such as the axillary, than in other diseases; this is connected with the stagnation of blood in the splanchnic area and the correspondingly small amount of blood in the cutaneous vessels.

In perforative peritonitis the initial shock nearly always depresses the temperature. But this is not an absolute rule; the variation probably depends on how much of the peritoneum is inundated by the contents of the bowel. The form of infection may influence the temperature, and a particularly virulent microbic invasion may so paralyze the power of resistance that there is less febrile reaction than in a less severe infection. In the vast majority of the cases of diffuse peritonitis the temperature is raised in some period of its course; it may be raised continuously, usually not to any great extent, and very seldom above 104° F. A relatively high temperature, especially in the early stages, is more likely to occur in the healthy and vigorous. A persistently low temperature may

[1] *Blood Pressure in Surgery*, Philadelphia, 1903.
[2] *Acta chir. Scandinav.*, 1921–1922, **54**, 559.
[3] *Arch. f. exper. Pharmak. u. Therap.*, 1912, **70**, 183.

depend on the severity of the infection and on failure of the organism to react, and is a grave sign.

Blood. There is anemia, but the erythrocyte count is not greatly diminished; probably the concentration of the blood accounts for this. In fulminating cases in which the resisting powers of the body are paralyzed by the intensity of the toxemia, leukocytosis is absent and there may be leukopenia. In less severe peritonitis there is a leukocytosis which may be extremely marked. It is of the ordinary polymorphonuclear neutrophile form. According to Locke[1] and Gulland[2] the glycogenic reaction seen in the polymorphonuclear neutrophiles is much more trustworthy, for it is present in cases of peritonitis with such a "brutal" infection that leukocytosis does not appear.

Blood-cultures.—Although the fatal results of peritonitis are usually considered to depend upon septicemia as well as on toxemia, and although organisms can often be found after death in the heart's blood, it does not appear that the presence of organisms in the blood during life has been proved. Libman[3] found that in 25 cases of peritonitis, mainly of intestinal origin, the blood was sterile, although in some instances the blood-cultures were made shortly before death.

The *urine* is scanty, high-colored, and may contain a small quantity of albumin, diacetic acid, and acetone. The most important point, however, is the large quantity of indican, which may rise from the normal 5 to 20 mg. in adults to 150 mg. Indicanuria takes some twelve to twenty-four hours to appear after the onset of perforative peritonitis.

According to Lennander, the urine contains the organisms responsible for the peritonitis. Their presence, especially as he states they may appear within twenty-four hours of the onset of the disease, may possibly in the future be of some value in directing the treatment. From the presence of peritonitis over the bladder micturition is painful, and usually urine is retained. Occasionally, on the other hand, micturition is more frequent than normal.

The *mental faculties* are often clear to the end, but sometimes they are somewhat obscured by the progressive toxemia. Sleeplessness is necessarily the rule, headache is common, and great anxiety and a painful form of restlessness are often present.

Death may be quite sudden and may follow almost immediately after copious vomiting. Death sometimes comes gradually from progressive asthenia.

The *duration* is very variable and depends on the cause and on the nature of the infection, the previous state of the patient, young and vigorous, or old and the subject of some exhausting disease, and on the treatment. Thus, in the most virulent and fulminating forms, as in some cases of appendicular and puerperal infection, death may occur in thirty-six to forty-eight hours from the onset, whereas the more usual and less severe forms generally last four, five, or even more days. A previously healthy boy may live through several days with severe

[1] *Boston Med. and Surg. Jour.*, 1902, **147**, 287.
[2] *Brit. Med. Jour.*, 1904, i, 880.
[3] *Johns Hopkins Hospital Bulletin*, 1906, **17**, 221.

peritonitis, while a patient with carcinoma of the stomach may only survive the onset of perforative peritonitis for eighteen to twenty-four hours. In pneumococcic peritonitis the duration may be considerably prolonged, as the peritonitis may become localized into residual abscesses, so that the symptoms abate without disappearing. Progressive fibrinopurulent peritonitis may go on for weeks.

Pneumococcic peritonitis presents some rather special features. The disease is much commoner in children than in adults. It may occur very early in life; Gossage[1] reported 4 fatal cases of primary pneumococcic peritonitis in infants under three months, and Dudgeon and Sargent its occurrence in a male aged seven weeks. Under the age of fifteen years it occurs more often in girls than in boys; among 234 cases in children 62, or 27 per cent., were males, and 172, or 73 per cent., females (Barling[2]); after that age it is rare, McCartney[3] indeed says that adults are immune. The following channels have been regarded as enabling the pneumococci to reach the peritoneum: (1) Through the blood-stream, the organisms being absorbed from pneumococcic foci in the thorax, the throat or ear; (2) from the stomach and intestines in inflammatory conditions, appendicitis, or foci in the abdominal viscera; (3) from the pleuræ through the diaphragm; and (4) through the Fallopian tubes. Probably infection of the peritoneum occurs by different channels but when associated, and in children, Rischbieth[4] finds that this is almost always the case with other pneumonic lesions, such as pneumonia, pleurisy, pericarditis, meningitis, otitis, and arthritis, and is probably hematogenous. On the other hand McCartney argues that primary pneumococcic peritonitis attacks females only and spreads from the vagina. Out of 56 cases reported with J. Fraser[5] 36 were primary and all in females under twelve years of age, and of the 20 secondary cases 12 were in boys and 8 in girls; no undoubted primary case of pneumococcic peritonitis has been reported in a boy. It is rare in pneumonia; in 4454 cases[6] of lobar pneumonia in patients over ten years of age in the hospitals of London there were 11 fatal cases, or 0.25 per cent. In most cases the peritoneum has been previously healthy; in a few instances there has been ascites due to cirrhosis or to chronic nephritis.

In about half the cases the peritonitis is encysted or localized; in the other half it is diffuse or widespread. A localized abscess may either be primary or a result of diffuse pneumococcic peritonitis. The exudate is like that of a pneumococcic empyema; it is highly fibrinous and prone to coagulate, yellowish green in color, and odorless. The character of the exudation renders thorough drainage of the peritoneum difficult. In some instances, however, a much more fluid exudate has been found. When the peritonitis is localized an abscess results which is usually below the umbilicus, and is particularly prone to point at the umbilicus.

[1] *Proc. Royal Soc. Med.*, London, 1908, i, (Med. Sect.), 64.
[2] *Practitioner*, 1912, **88**, 557.
[3] *Jour. Path. and Bacteriol.*, Edin., 1923, **26**, 507.
[4] *Quart. Jour. Med.*, 1910–1911, **4**, 205.
[5] McCartney and Fraser: *Brit. Jour. Surg.*, Bristol, 1922, **9**, 479.
[6] Statistics of Hadley, Pasteur, Fawcett, Owne, Gossage: *Proceedings of the Royal Society of Medicine*, London, 1908, i, (Med. Sect.), 61 et seq.

Clinically the disease may run a very acute course and prove fatal in two or three days, or death may not occur until the sixth or seventh day. There may be the following stages: (1) Without prodromal symptoms there is an acute onset with vomiting, followed by signs of peritonitis, often mainly in or near the pelvis, so that appendicitis may be diagnosed. (2) After a few days the symptoms subside, the temperature falls, but diarrhœa is usually present, and typhoid fever may be suspected. (3) A prolonged stage in which residual abscesses may form, usually in the upper part of the abdomen, giving rise to continued fever and imitating tuberculous peritonitis. Herpes labialis may occur.

The *prognosis* in encysted pneumococcic peritonitis is fairly good but very grave in the diffuse form; Rohr[1] found that recovery occurred in 86 per cent. of the encysted and in 11 per cent. of the diffuse form.

Gonococcic Peritonitis.—The gonococcus alone, *i. e.*, in pure culture, is capable of setting up diffuse peritonitis (Cushing[2]). When the normal resistance of the peritoneum is diminished by menstruation or by cold, gonococci in the Fallopian tubes have a better chance of infecting the peritoneum. Gonococci enter the peritoneum from the ostia of the Fallopian tubes, but gonococcic peritonitis has followed leakage from a pyosalpinx during removal by operation. In males infection is said to travel up the lymphatics of the spermatic cord.

The disease is very rare in men and its frequency in women has not yet been established by extensive statistics; but diffuse gonococcic peritonitis is not common. In 1907 Goodman[3] collected 75 cases, but only 30 of these had been established by bacteriological examination at autopsy or operation. It may attack girls under puberty, and it is highly probable that it is often overlooked. It usually follows or precedes menstruation, and may appear shortly after delivery. The lesions are comparatively slight; there is a dry, fibrinous exudate without pus or serum, and the peritoneum is uniformly injected in the diffuse cases.

Clinically, gonococcic peritonitis comes on suddenly with great severity, which usually becomes greatly mitigated in twenty-four or forty-eight hours. Comby[4] speaks of the condition as one of peritonism rather than of peritonitis. It appears to be more fatal in children than in adults; the mortality in children has been estimated at 20 per cent. It may imitate appendicitis, as it mainly affects the lower part of the abdomen. Abdominal distention is usually not marked, and muscular rigidity is absent. Its existence should be suspected in the presence of gonorrhœa when the peritonitis is mainly in the lower part of the abdomen. At the onset of the disease the gonorrhœal discharge may be slight, and careful examination is necessary to avoid overlooking it. Opinion as to advisability of operative interference has varied; Wildenskov[5] finds that the mortality is much higher in the cases not operated upon.

Puerperal Peritonitis.—The infection gains entry through tears or wounds of the genital passages, and is more frequent in primiparæ than

[1] *Mitt. a. d. Grenzgeb. d. Med. u. Chir.*, 1911, **23**, 658.

[2] *Johns Hopkins Hospital Bulletin*, 1899, **10**, 75. (This article contains the detailed history of gonococcic peritonitis.)

[3] *Annals of Surgery*, 1907, **46**, 111.

[4] *Arch. mal. d. enfants*, 1901, **4**, 512.

[5] *Ugesk. f. Læger.*, 1902, **82**, 1227.

in multiparæ. It is not uncommon in criminal abortion. The infection spreads from the genital organs by the lymphatics, and may be localized or widespread in the peritoneal sac. The organism is most commonly *Streptococcus pyogenes*, but staphylococci or the gonococcus may be the causal agent. The exudation may be purulent, sanious, or putrid.

Clinically there is grave intoxication and usually diarrhœa; vomiting is less prominent than in other forms; meteorism is marked, partly no doubt from the weakened abdominal walls; and a high mortality, which may be correlated with the presence of *Streptococcus pyogenes*. At its onset the lochia may be offensive and the mammary secretions be suppressed. Complications are prone to occur, and include septicemia, empyema, pericarditis, arthritis, and phlebothrombosis.

Biliary peritonitis without obvious perforation of the biliary tract, which should be distinguished from choleperitoneum (vide p. 908) has a sudden onset simulating appendicitis or perforative peritonitis, and according to Meyer-May,[1] who collected 20 cases, depends on changes in the gall-bladder, such as distention, inflammation, gall-stones, and on a sudden increase in the pressure of the bile. Johannson[2] suggested that the escape of bile took place through the hernial protrusions of the mucosa ("Luschka's canals") into the walls of an inflamed gall-bladder. Vomiting occurs in more than one-half the cases, but jaundice is absent. The most satisfactory treatment is cholecystectomy.

Diagnosis.—In characteristic cases the association of the prominent symptoms of acute pain, tenderness, distention, and immobility of the abdomen, vomiting, constipation, prostration and collapse, together with the history, make the existence of acute peritonitis clear. But in many cases the decision is far from easy. When peritonitis supervenes late in the course of chronic nephritis it may be almost latent, when it occurs in typhoid fever it may be difficult to distinguish from tympanites, and in acute intestinal obstruction its manifestations are combined with and obscured by those of the primary disease. Further, the symptoms may be almost entirely masked by opium or morphine. In some cases the majority of the signs and symptoms may be absent, although there is advanced peritonitis. This masked or latent form of peritonitis may occur in patients in the last stages of exhausting diseases, such as cancer. After operations on the abdomen the only evidence of peritonitis may be vomiting and a rapid pulse.

Diagnosis of Acute Peritonitis from Conditions Simulating It.—In hysteria a condition of peritonism may occur and give rise to considerable anxiety, as the diagnosis between it and genuine peritonitis occurring in a hysterical patient may be difficult. The history of the patient and any concomitant nervous symptoms must be taken into account. As an important point the occurrence of exactly similar attacks in the past should be specially noted. In such cases there is cutaneous hyperesthesia; deep tenderness is not more marked than the superficial hyperesthesia, and may disappear if the patient's attention be distracted.

Severe *colic*, whether due to lead, constipation, or the passage of a

[1] *Presse méd.*, Paris, 1924, **32**, 883.
[2] *Rev. de chir.*, Paris, 1912, **46**, 892.

gall-stone or renal calculus, may to some extent imitate acute peritonitis. In colic there is, as a rule, no real tenderness, and the pain may be relieved by firm pressure. In severe lead colic there may, however, be tenderness, but the pupils are often unequal and there may be tenderness over the vagus in the neck (T. Oliver[1]). In a doubtful case with abdominal tenderness the possibility of lead-poisoning should always be considered. In colic due to the passage of a calculus vomiting occurs, but it is rare in the other forms. The history and examination for evidence of lead-poisoning, renal, or hepatic disease should be carefully considered. A raised temperature at the onset is strongly in favor of peritonitis and against ordinary colic. Colic, however, is more likely to be confused with the causes of peritonitis—such as appendicitis—than with the disease itself. The rare and puzzling condition of enteralgia may also imitate peritonitis; here again the history of repeated similar attacks is of importance. Extremely acute enterocolitis is accompanied by the same collapse as in peritonitis, but there is marked diarrhœa and the pain is of a colicky character.

Tympanites should be readily distinguished from acute peritonitis by the absence of tenderness and vomiting.

In acute mechanical intestinal *obstruction* acute peritonitis supervenes after some three or four days, and, conversely, acute peritonitis produces intestinal paralysis and the symptoms of obstruction, so that the diagnosis as to the primary lesion may be difficult. In acute obstruction the temperature is not raised, and the abdomen is not tender or rigid before the onset of secondary peritonitis. In mechanical obstruction feces and wind are not passed, while in peritonitis an enema will often bring some away. In mechanical obstruction vomiting is more profuse, the pain is colicky and not continuous, as in peritonitis.

Extensive *hemorrhage* into the peritoneum, usually due to rupture of an ectopic gestation, may imitate perforative peritonitis very closely; in fact, the manifestations in both instances are those of shock. A similar clinical condition of peritonism may follow hemorrhage into the mesentery, torsion of an undescended testis, of an ovarian cyst, of a floating kidney, or of a wandering spleen. Rupture of an abdominal aneurism and embolism of the superior mesenteric artery have imitated acute peritonitis (Osler).

Acute hemorrhagic pancreatitis may imitate acute perforative peritonitis; great collapse, abdominal distention, complete constipation, and vomiting follow the sudden onset of pain in the epigastric region. If the abdomen be opened, turbid fluid and fat necrosis may be found. It may be noted, however, that fat necrosis may be due to the escape of pancreatic fluid through the perforation of a duodenal ulcer,[2] so that its discovery, although almost pathognomonic of pancreatitis, does not absolutely exclude perforation. In pancreatitis there is extreme feebleness of the pulse, the temperature is often not raised, and the symptoms are more suggestive of mechanical obstruction than of peritonitis.

Acute inflammatory conditions in the thorax, such as *lobar pneumonia*

[1] *System of Medicine* (Allbutt and Rolleston), 1906, **2**, part i, 1045.
[2] White, *Archives of the Pathological Institute of the London Hospital*, 1906, i, 48.

or *pleurisy*, may imitate peritonitis. The sharp pain of pleurisy has been mistaken for perforation of a gastric ulcer or of a gangrenous appendix. Difficulty is especially likely in children in whom the appearance of the physical signs of pneumonia is often much delayed. In pneumonia the respirations may be jerky and grunting. The rigidity of the abdominal muscles sometimes seen in pneumonia, especially in children, relaxes between the respirations, and may even disappear on prolonged and deep pressure (Clogg[1]), while the referred pain of thoracic disease is mainly superficial and not increased on deep pressure, as in peritonitis. The temperature may be of some assistance; low at the onset of perforative peritonitis, it then rises, but may fall after some hours, although the patient's condition is not improved. It thus differs from the continuous fever of pneumonia. Indicanuria is in favor of peritonitis. Tuberculous peritonitis in rare cases comes on with such acute symptoms in children as to imitate very closely peritonitis due to appendicitis.

In women about the menstrual period sudden acute pain may imitate perforation of a hollow viscus or rupture of an ectopic gestation. The symptoms pass off, as a rule, but are alarming enough at the time. The underlying cause has been thought to be hemorrhage into the ovary. In one case attended by great temporary collapse the real cause appeared to be synthetic drugs taken to relieve the initial pain.

Uremia may imitate diffuse peritonitis, and uremic ulceration of the intestine may lead to perforative peritonitis, and hematogenous peritonitis may supervene in chronic renal disease.

In very rare instances acute abdominal symptoms imitating appendicitis or even peritonitis supervene in *Addison's disease* (Nattan-Larrier[2]) and appear to be allied to the vomiting in that disease.

Malaria may cause symptoms suggesting peritonitis. H. C. Parsons,[3] who collected cases in Salonica during the war, found that there is a polymorphonuclear leukocytosis, and explains this peritoneal syndrome by extension of acute perisplenitis to the diaphragm. The diagnosis depends on the detection of the parasite.

Acute *osteomyelitis* of the spine may imitate peritonitis.

When the presence of peritonitis has been determined it is most important to diagnose the cause and to decide whether it is due to perforation of a gastric, duodenal, or an intestinal ulcer, to appendicitis, to rupture of an abscess, and, if so, where, to gonococcic or pneumococcic infection, and so on; for on the correct diagnosis of the cause depends the site of the abdominal incision. As bearing on the cause of peritonitis the following points may be taken into consideration:

Age.—In children peritonitis of sudden onset is most commonly due to fulminating appendicitis; but pneumococcic and gonococcic peritonitis must be considered.

Sex.—In young women perforated gastric ulcer and pelvic infection are the most common causes.

[1] *Clin. Jour.*, London, 1906, **29**, 93.
[2] *Clinique médicale de l'Hôtel-Dieu*, 1906, **5**, 250.
[3] *Contributions to Medical and Biological Research dedicated to Sir W. Osler*, 1919, **2**, 1149.

History.—Symptoms of dyspepsia in young women at once suggest a perforated gastric ulcer, while in patients about fifty years of age carcinoma of the stomach with perforation should not be forgotten. When peritonitis comes on suddenly in a patient who has had gastro-enterostomy done for gastric ulcer, the possibility of perforation of a peptic jejunal ulcer should be thought of. The existence of typhoid fever, advanced kidney disease, or of a pelvic abscess will indicate the probable starting-point of the peritoneal infection.

The position in which the pain is first felt should be considered, but it is by no means a certain guide, for, although pain starting in the right iliac fossa naturally suggests appendicitis, pain in this situation may be due to perforation of a gastric or duodenal ulcer.

The sudden onset of peritonitis in a person in good health up to that time may be due, especially in children, to fulminating appendicitis, in young women to perforation of a latent gastric ulcer, and in men to perforation of a duodenal ulcer which is relatively more often latent than a gastric ulcer is in women.

Prognosis.—This is very bad. Statistics differ very much in the percentages of mortality, because, as has been pointed out, a case which at operation one surgeon may describe as diffuse another would regard as general or universal. In 100 cases at the London Hospital there were 70 deaths and 30 recoveries (Treves), but the different forms of peritonitis vary so much in their severity that no conclusion of any value can be obtained from statistics in which cases of the various kinds are indiscriminately included. Other things being equal, peritonitis is more fatal at the two extremes of life. The previous health of the patient, the presence of disease elsewhere, cachexia, and alcoholism, of course, have a bearing on the prognosis.

As the fatality of peritonitis depends on toxemia and septicemia, the prognosis to some extent varies with the degree of the toxic symptoms; the cases of acute peritoneal sepsis in which there is very little reaction on the part of the peritoneum are almost always fatal. Bad as the prognosis is in purulent peritonitis, it occasionally happens that the inflammation becomes localized and an abscess results. A very rapid pulse, a persistently low temperature, abdominal distention, and absence of leukocytosis give a bad prognosis.

From a bacteriological point of view peritonitis due to Dudgeon and Sargent's white staphylococcus is the most benign form, while that due to gonococci is comparatively mild. In pneumococcus peritonitis the prognosis is graver than in the forms just referred to, but is not so serious as in those now to be mentioned. The commonest cause of peritonitis is infection with virulent colon bacilli; if present alone in the peritoneal cavity at a distance from the infecting focus the outlook is bad; and if all the phagocytes are degenerated the prognosis is practically hopeless. If *B. coli* and the white staphylococcus are associated, the outlook is not so bad, but is still very serious. The *Streptococcus pyogenes* gives rise to the most acute and fatal peritonitis. Peritonitis due to the *B. pyocyaneus* is hardly less fatal (Dudgeon and Sargent).

The prognosis is almost necessarily fatal in perforative peritonitis

unless operated upon; when operation has been performed the outlook is much better in traumatic rupture or bullet wounds of the intestine than in perforation due to disease. Similarly the prognosis is better in perforation of a gastric or duodenal ulcer than in perforation of an intestinal ulcer lower down, because, as shown by Cushing and Livingood,[1] the number of colon bacilli steadily diminishes from the ileocecal valve to the stomach, and the duodenum is often sterile when empty. The interval between the onset of peritonitis and the time at which the operation is performed has an important bearing on the prognosis; operation within twelve hours of the onset should be successful, while an interval of twenty-four hours makes the outlook very grave.

Treatment.—Prophylaxis.—Under this heading the briefest reference only need be made to the desirability of preventing or curing the causes of general peritonitis, such as gastric or intestinal ulceration, appendicitis, pelvic inflammation, and intra-abdominal abscesses. Among these the importance of timely surgical interference in acute appendicitis pelvic inflammation, and intra-abdominal abscesses. The importance of timely surgical interference in acute appendicitis cannot be exaggerated. Strict precautions should always be taken to avoid the introduction of organisms into the peritoneal cavity when the abdomen is tapped for the relief of ascites or when laparotomy is performed.

Various prophylactic measures have been adopted in order to immunize the peritoneum against probable infection during the course of laparotomy. Injection of vaccines of streptococci and *Bacillus coli* ten and three days before on abdominal operation, followed the night before the operation by the injection of 8 cc. of a 2 per cent. solution of nucleic acid, to provoke a leukocytosis, gave good results (D. Wilkie[2]). Horse serum and nucleate of sodium have also been employed instead of nucleic acid.

Surgical Treatment.—The great majority of cases depend on infection from some local focus in the abdominal cavity, and are therefore rightly treated by removal of the cause. In the small minority of cases in which the infection is hematogenous, operative interference is not so necessary, but is required to drain a local abscess, as may be seen in pneumococcic peritonitis.

The objects of laparotomy are: (1) to remove the focus of infection, such as a perforated appendix, or to prevent continued reinfection, as is done in suture of a perforated ulcer; and (2) to give exit to the inflammatory exudate and if necessary provide efficient drainage. In order to prevent absorption of bacteria by the lymphatics of the diaphragm, the pelvis is lowered and the patient placed in the semi-sitting (Fowler's) position, at an angle of 35 to 40 degrees, both before operation and for some days afterward. Drainage tubes, gauze drains which by the suction action of capillarity counteract the effects of gravity or continuous irrigation by Carrel's tubes are the usual means of securing efficient drainage.

When the intestines are greatly dilated from paralysis, the danger

[1] *Contributions to the Science of Medicine by the pupils of W. H. Welch*, 1900.
[2] *Brit. Med. Jour.*, 1923, ii, 189.

of fatal toxemia from absorption of the foul contents of the bowel may be met by emptying the intestines. This can be done at the time of the operation by incising the bowel and expressing its contents, or, in more urgent cases, by inserting a Paul tube into the intestine and leaving it for some hours *in situ*, or by jejunostomy (V. Bonney). In spreading hypogastric peritonitis leading to pelvic peritonitis and secondary paralysis of the pelvic colon (ileus duplex) Handley[1] has saved life by ileo- or jejuno-colostomy combined with cecostomy. Lymphaticostomy or external drainage of the thoracic duct in the neck has been employed to diminish the toxemia due to the entrance of toxic bodies into the left subclavian vein (Costain[2]). J. G. Jones[3] treats cases of grave postoperative peritonitis by slow irrigation of the affected area of the peritoneum; saline solution is introduced through a Carrel's tube at the rate of 1 drop a second and removed together with exudate by negative pressure into a Wolff's bottle. Other methods have been employed, such as injecting purgatives of magnesium sulphate by a syringe directly into the intestine during the operation after removing some of its contents; by hypodermic injections of eserine or pituitrin, or by both together, which is said to be more effective than either alone (Kerr Cross[4]); but from analyses of 162 cases of pelvic operations, Martztoff[5] finds that the combination of eserine and strychnine has not any beneficial effect on postoperative tympanites. The administration of enemas, often quite unsuccessful; or the administration of calomel in 1-grain doses every hour until the bowels act were formerly employed. The purgative treatment of peritonitis, however, is useless when the intestines are paralyzed, and should only be adopted after operation and removal of the infecting focus. If employed before operation, it does harm by spreading the infection.

In order to prevent peritoneal adhesions Behan[6] advocates the application to the injured peritoneal surfaces of a paste of pure lanolin containing 5 per cent. of boric acid; it tends to inhibit the formation of adhesions by protecting the surfaces for several hours during which the endothelium is so far repaired that adhesions cannot form; if, however, the endothelial covering does not return, adhesions will form. Peristalsis should be kept up by drugs, such as eserine, strychnine, and magnesium sulphate, and heat rather than cold applied to the abdomen.

Transfusion—To meet the urgent need for fluid and to combat collapse and toxemia, enemas or a continuous rectal administration of saline solution have been given but has been condemned by Babcock[7] as providing a fecal decoction; the introduction of saline solution intravenously or subcutaneously has also been extensively employed. Of the last two the subcutaneous method is the more convenient and can be frequently repeated if needed. For intravenous injection the solution should be of the strength of 1 dram of salt to 1 pint of water (0.6 per cent.) and after

[1] *Brit. Jour. Surg.*, 1925, **12**, 417.
[2] *Surg., Gynec., and Obst.*, 1923, **36**, 365.
[3] *Guy's Hosp. Rep.*, 1925, **75**, 222.
[4] *Brit. Med. Jour.*, 1924, i, 9.
[5] *Bull. Johns Hopkins Hosp.*, 1924, **35**, 370.
[6] *Am. Jour. Med. Sci.*, 1920, **160**, 375.
[7] *Internat. Clinics*, Phila., 1925, 35th ser., **4**, 181.

Bayliss' method[1] for shock and hemorrhage has been fortified by the addition of gum acacia (7 per cent.) in order to prevent the fluid leaving the vessels rapidly; it should be introduced by gravitation, the fluid in the reservoir being kept at 115° F. By filling the vascular system, absorption of poisons from the peritoneal cavity is inhibited, the current of the stream between the peritoneal cavity and the circulation being reversed. Crile[2] believing that the general symptoms of peritonitis are due to acidosis advises enemas of 5 per cent. glucose and 5 per cent. sodium bicarbonate and subcutaneous injections of 2500 to 6000 cc. saline solution in twenty-four hours. Intravenous injection of 8 per cent. of glucose has been given by the continuous drop method (Matas[3]) and as much as 18 pints have been introduced in the twenty-four hours (Moynihan[4]); Lilian Farrar[5] has given a 20 per cent. solution of glucose intravenously, and insulin therapy has been employed to supplement the injection of glucose by enabling the tissues to make full use of it (Thalhimer[6]). Saline solution may cause pulmonary œdema; toxic effects have followed some injections of gum acacia solution, and auto-agglutination of the red blood cells, thrombosis of the pulmonary vessels, and anaphylaxis have been described. From an extensive experimental comparison of intravenous transfusions for shock, F. C. Mann[7] found that much better results were obtained from transfusions of blood or blood serum than from gum solutions.

Medical Treatment.—The patient's shoulders should be raised with pillows, so that the exudation will gravitate toward the pelvis rather than toward the diaphragm. If tenderness is extreme the bedclothes may be kept off the abdomen by a cradle. The abdomen should be manipulated as little as possible, both because of the tenderness and because infection may thus be spread. The mouth should be frequently cleaned and kept moist. Purgatives must be prohibited, for by promoting peristalsis they increase pain and spread infection more widely in the peritoneal cavity.

No food or fluid should be given by the mouth, and the urgent thirst should be relieved by enemas of saline solution. Vomiting may be treated by washing out the stomach. It is doubtful if bismuth, hydrocyanic acid, and drugs that calm an irritable stomach in other diseases are worth giving. Tympanites is difficult to relieve; enemas containing turpentine may be tried; or a long rectal tube may be passed every three hours and left *in situ* for half an hour.

The administration of opium in acute peritonitis has given rise to a good deal of discussion, but generally speaking it is now given for humanitarian reasons, and not with the expectation of any permanent benefit. The reasons for giving opium or morphine are the severity of the pain, and also, it was formerly urged, to keep the intestine at rest and so prevent further spread of the infective process. It is also given when the condition of the patient appears hopeless, so as to relieve pain and suffering. Crile,[8] however, gives morphine until the respirations fall to 13 per

[1] *Proc. Roy. Soc.*, 1916, **89**, 390.
[2] *Jour. Am. Med. Assn.*, 1919, **73**, 1655.
[3] *Ann. Surg.*, 1924, **79**, 643.
[4] *Brit. Med. Jour.*, 1925, i, 393.
[5] *Surg., Gynec. and Obst.*, 1921, **32**, 320.
[6] *Jour. Am. Med. Assn.*, 1923, **81**, 383.
[7] *Am. Jour. Physiol.*, 1919, **50**, 86.
[8] *Jour. Am. Med. Assn.*, 1919, **73**, 1655.

minute. The objections to opium are weighty. It masks the symptoms and so should never be given before a diagnosis has been made. But after a diagnosis has been arrived at, and especially when the patient is too ill to stand operation, opium is not uncommonly given. Even in these conditions it is undesirable, for since it induces intestinal paralysis and inhibits phagocytosis (Dudgeon and Sargent[1]), it may just turn the scale against recovery.

Various local applications to the abdomen have been employed to relieve pain, such as hot and cold fomentations, the ice-bag, turpentine stupes, but often the slight pressure they exert gives rise to pain, and it is doubtful how much good is done in this way.

Collapse may be treated by the external application of warmth, hot packs, bandaging the limbs, and the hypodermic injection of strychnine or pituitary extract; epinephrine has proved disappointing.

Serum Treatment.—In 25 cases of peritonitis due to appendicitis, treated by injections of the serum of a horse immunized against thirty-one strains of *B. coli*, recovery occurred in 9, or 36 per cent., and improvement was produced in all the others (Makins and Sargent[2]). Wilkie[3] treated 6 cases of very severe peritonitis with intravenous injections of human immune serum from patients recovering from similar infections and obtained 3 recoveries. Multivalent antistreptococcic serum has been tried in numerous cases, especially in puerperal septicemia, unfortunately in the majority of cases without success.

ACUTE CIRCUMSCRIBED PERITONITIS

Acute circumscribed or localized peritonitis may be conveniently divided into (1) non-suppurative and (2) suppurative.

Non-suppurative acute circumscribed peritonitis is extremely frequent and is due to extension of inflammation to the peritoneum. This is usually from organs in the abdominal cavity covered by peritoneum, such as the vermiform appendix, the intestines, the female genital organs, the gall-bladder and liver; but acute inflammation of the pleura or pericardium may spread through the diaphragm to the surfaces of the spleen and liver; the results of this process are comparatively often seen in adhesions found after death on both sides of the diaphragm. A good example is that produced by an infarct in the spleen. There is pain on breathing like that of pleurisy, local tenderness, and from organization of the localized exudate adhesions frequently follow.

The chief clinical manifestation is pain, which may vary in intensity but is confined to one area, and is made worse on pressure. A friction rub may be audible over the spleen or liver. Acute circumscribed peritonitis may, by producing local paralysis of a coil of intestine, set up acute obstruction; this may occur as the result of acute cholecystitis. The main importance, however, of sharply circumscribed acute peritonitis lies not so much in its immediate effects as in results

[1] *The Bacteriology of Peritonitis*, 1905, p. 188.
[2] *Trans. Clin. Soc. London*, 1907, **40**, 146.
[3] *Jour. Path. and Bact.*, Cambridge, 1910, **14**, 270.

which it produces by the formation of local adhesions. By enclosing the affected area and shutting it off from the general peritoneal cavity, rupture of a perforating ulcer or of an abscess into the general peritoneal cavity may be prevented. On the other hand, the evil effects of a past attack of acute circumscribed peritonitis are shown by the occurrence of internal hernia due to strangulation of the intestine by bands and by "adhesion dyspepsia."

The *treatment* is mainly symptomatic and directed to the relief of pain by external applications, such as hot fomentations or ice, the patient's feelings being consulted as to which is most effective. Opium or belladonna may be applied to the abdomen, or, if the pain be obstinate, leeches may be employed. The underlying conditions should, when possible, be treated.

Acute Pericolitis.—This occurs in a number of conditions, and necessarily forms part of diffuse peritonitis and of various intraperitoneal abscesses and localized inflammations. As a descriptive heading, however, acute pericolitis should be confined to inflammation of the serous coat due to causes arising in the colon itself. Windscheid[1] first described cases under the name of pericolitis in 1889.

Etiology.—It may be due to causes which allow microörganisms to traverse the walls of the colon, such as acute inflammation, ulceration, injury, or the passage of sharp foreign bodies through the walls of the colon. There is often a history of previous constipation, but constipation is so common and pericolitis so comparatively infrequent that some further factor appears to be necessary. This additional factor is probably stercoral ulceration, especially in acquired diverticula of the colon. The writer has recorded several examples,[2] and Rixford[3] described a closely allied condition in which inflammation of the appendices epiploicæ is due to infection conveyed from the colon. As stercoral ulcers and false diverticula are more often present in the sigmoid flexure and descending colon, pericolitis is commoner in these parts of the large intestine. It is spoken of as *perisigmoiditis* and *pericolitis sinistra*, but it may occur in the transverse or descending colon, especially at the flexures, where, from organization of adhesions (chronic pericolitis), the bowel may become narrowed, fixed, or kinked. Acute pericolitis may resolve, become chronic, or go on to the formation of a pericolic abscess. This condition is described as diverticulitis on p. 629.

Epiploitis.—Epiploitis, or inflammation of the great omentum, is of course common in intraperitoneal inflammations on account of the tendency of the omentum to become attached to any focus of infection. It has been especially described as a result of abdominal operations in which silk ligatures have been applied to the omentum. According to P. Picot[4] 76 per cent. of the postoperative cases of epiploitis are due to radical herniotomy; usually the symptoms appear some weeks after the operation, but the interval may be longer; it has been met with two

[1] *Deutsch. Arch. f. klin. Med.*, Leipsic, 1889, 45, 233.
[2] *Lancet*, 1905, i, 854.
[3] *California State Jour. Med.*, October, 1904, p. 296.
[4] *Thèse de Bordeaux*, 1924.

years after appendectomy (Walther[1]). Cobb[2] described epiploitis due to a needle which appeared to have entered from the umbilicus. The condition of the omentum varies; it may be thickened and rolled into a firm mass showing inflammatory changes, and it may be adherent to other structures, or free. In a woman under my observation two radical cures for hernia had been done in 1899 and 1900; in 1903 the appendix was removed, and about two months later a definite, firm abdominal tumor appeared on the left side and a hectic temperature developed, but on laparotomy there was no abscess formation; part of the omentum was rolled up into a round mass which microscopically showed developing connective tissue and some diminution in the number of fat cells. In rare instances intestinal obstruction may follow. The inflammatory process may go on to the formation of an abscess.

The *symptoms* usually come on gradually, with fever, pain, constipation, and the presence of definite resistance or a tumor in the abdomen. The tumor may be lumpy, firm, adherent to the abdominal wall, tender, and imitate a new growth. It may be chronic and eventually undergo resolution, but from contraction of adhesions the intestines may become kinked or otherwise obstructed. Epiploitis of this nature is rare, but if the conditions after which it occurs be borne in mind, the diagnosis should not be difficult.

Treatment in the early stage, when there is inflammation but not necessarily an abscess in the omentum, consists of soothing local applications. If fever persists and it appears probable that suppuration has occurred, laparotomy is the only course. Removal of the infected omentum may be followed by attacks of nausea, vomiting and urobilinuria, ascribed to thrombosis of the intrahepatic radicles of the portal vein, and Hansen[3] recommends that resection of the omentum should be performed through healthy tissue.

There are transitional forms between non-suppurative and suppurative acute circumscribed peritonitis. It is not very rare in appendicitis to see a tumor-like swelling, which gradually disappears in a few days without any evidence that pus has been discharged into the bowel. The swelling is probably due to adherent intestines, with some inflammatory exudate enclosed between the coils of the bowel. In other cases, *e. g.*, epiploitis, which at first show exactly the same features, an abscess eventually forms.

SUPPURATION IN THE MESENTERY AND OMENTUM

Suppuration in the mesentery is usually secondary to disease of the intestine. As the result of infection conveyed from the small intestine, a mesenteric gland may suppurate, or pyogenetic infection may be engrafted on an old tuberculous adenitis. In cases of suppurative inflammation of the mesenteric veins there may be pus between the

[1] *Bull. et mém. Soc. de chir. de Paris*, 1905, **31**, 275.
[2] *Boston Med. and Surg. Jour.*, 1907, **157**, 18.
[3] *Acta chir. Scandinav.*, 1924, **58**, 285.

layers of the mesentery. Suppuration may also spread from the appendix into the mesentery. Barling[1] has published a series of cases, and has summarized the clinical aspect of the tumor; it is usually close to the umbilicus, mainly to the left side; when of considerable size it is practically fixed, but when of small size the swelling may not be palpable or if it can be detected is movable. Rupture of the abscess may set up general peritonitis.

Omental abscesses are rare. As has been mentioned above, suppuration may supervene after epiploitis. Thus, several abscesses have been found in the omentum more than a year after an operation.

PERIGASTRIC ABSCESS

By a perigastric abscess is meant one that is due to infection from the stomach but does not come in contact with the under surface of the diaphragm, and, strictly speaking, is therefore not included in the more striking category of subphrenic abscess. Suppuration due to disease of the pancreas, gall-bladder, or liver may be in contact with the stomach, but these abscesses should not be described as perigastric.

Etiology.—In exceptional instances a simple perigastric abscess may be due to a minute perforation in the stomach wall, such as is produced by a sharp foreign body, or to slight leakage from a gastric ulcer, but, generally speaking, perforation of a gastric ulcer is followed by a gaseous subphrenic abscess. A perigastric abscess occurs in from 3 to 5 per cent. of all cases of gastric carcinoma (Fenwick[2]) and is a late event. It is more often met with, so far as personal experience goes, in connection with rapidly growing and necrotic growths near the cardiac end; suppuration may then invade the left lobe of the liver. An abscess may form between the greater curvature of the stomach and the colon and then open into the large bowel, or may arise between the abdominal wall and the anterior surface of the stomach, and even point anteriorly or track down to the umbilicus. When a growth on the posterior wall of the stomach perforates, an abscess may form in the lesser sac of the peritoneum. The pus may be offensive, and if the abscess be opened during life, food may be discharged.

Signs and Symptoms.—A superficial perigastric abscess may be palpable as a definite swelling, and even give rise to a projection and to reddening of the skin. But usually, especially in gastric carcinoma, a perigastric abscess gives few physical signs; any increased resistance may be indistinguishable from that of the growth, and as fever occurs in 50 per cent. of the cases of gastric carcinoma (Osler and McCrae[3]) it is no proof of perigastric abscess.

Diagnosis.—It is practically impossible to diagnose between a perigastric abscess and the circumscribed form of phlegmonous gastritis, which is the same as an abscess in the walls of the stomach. A rapidly growing retroperitoneal sarcoma or hypernephroma may form a tender swelling in the left hypochondrium and imitate a perigastric abscess.

[1] *Clinical Journal*, London, 1907, **30**, 62.
[2] *Cancer and Tumors of the Stomach*, 1902, p. 46.
[3] *Cancer of the Stomach*, 1900, p. 46.

PERICOLIC ABSCESSES

Abscesses due to infection from the bowel may occur in the immediate neighborhood of the large intestine from a number of causes: (1) From ulceration of the mucous membrane of the bowel, due to dysentery, accumulation of feces (stercoral), or, more rarely, to other factors, and by perforation by foreign bodies, circumscribed peritonitis may be set up, and sometimes a localized abscess may result. The abscess may be intraperitoneal, and may open into the bowel (exogenous ulceration) or into the peritoneal cavity, or may be retroperitoneal. (2) The mucous membrane of false diverticula of the colon, which are more often found in connection with the sigmoid flexure, may, as the result of the accumulation of fecal material inside them, undergo ulceration; perforation of these diverticula may lead to an abscess in the immediate neighborhood. (3) Suppuration may occur in connection with a carcinoma of the large intestine. This may depend on perforation of the growth itself, on the passage of microörganisms through the floor of stercoral ulcers above the malignant stricture, or on perforation of these ulcers. The resulting tumor may be of considerable size, and on the right side must be differentiated from appendicitis with much inflammatory swelling, actinomycosis, and hyperplastic tuberculosis of the cecum. An abscess formed in connection with a malignant stricture of the bowel may extend and open into the urinary bladder or even externally; rupture into the peritoneal cavity, however, appears to be infrequent. (4) Small but sharp foreign bodies present in food may penetrate the wall of the colon and set up a fecal abscess in an appendix epiploica (Bland-Sutton[1]). This accident is more likely to occur in fat persons, for in thin individuals the foreign body more readily escapes into the peritoneal cavity.

The *symptoms* are abdominal pain, tenderness, resistance, local prominence or distention, and perhaps a tumor, usually on the left side and suggesting left-sided appendicitis or even a new growth. Constipation is commonly present, and also, not infrequently, vomiting. The abscess may increase in size and may rupture into the peritoneal cavity; the acute onset of peritonitis following on a period of pain and constipation may then suggest perforation above a malignant growth of the colon. Power[2] says that in some instances the abscess may become stationary, and from thickening of its walls give rise, for a time at least, to few clinical manifestations. The abscess may rupture into the intestine (Mayor[3]), or even into the urinary bladder, or externally (Patel[4]).

The *diagnosis* of these pericolic abscesses may be difficult, as from their comparative rarity some commoner condition, such as appendicitis in an unusual position, fecal accumulation, or malignant disease of the colon, may be suspected.

The *treatment* is purely surgical.

[1] *Lancet*, London, 1903, ii, 1148.
[2] *Brit. Med. Jour.*, 1906, ii, 1171.
[3] *Rev. méd. de la Suisse Rom.*, Genève, 1893, **13**, 421.
[4] *Rev. de chir.*, Paris, 1907, **36**, 402, 698.

RESIDUAL PERITONEAL ABSCESSES

Residual peritoneal abscesses may occur in patients who have recovered from more or less general acute peritonitis. These abscesses may be found in any part of the abdomen, but are most often seen in the loins, pelvis, over the right lobe of the liver, or around the spleen. In tuberculous and pneumococcic peritonitis, and in suppuration in connection with the gall-bladder, abscesses may point at the umbilicus.

RETROPERITONEAL ABSCESSES

Suppuration behind the peritoneum may be due to many causes, and when starting in one spot may spread to a considerable distance along the fascial planes by the lymphatics. A retroperitoneal abscess may be in contact with the diaphragm. A psoas or iliac abscess due to tuberculous disease of the spine is, of course, retroperitoneal, but belongs to a somewhat different category, as does an iliac abscess due to calculous or tuberculous disease of the kidneys. Retroperitoneal suppuration may also be set up by disease of the bones of the pelvis or of the ribs. An abscess sometimes follows injury, especially in the neighborhood of the kidneys, and may be caused by minute rupture of viscera, or follow a hematoma. In other instances infection conveyed from the intestines to the retroperitoneal glands may result in the formation of an abscess. Perforation of viscera in situations where they are uncovered by peritoneum may be followed by retroperitoneal suppuration. Thus traumatic rupture, a penetrating bullet wound, or perforation of a stercoral ulcer in the colon may lead to a pericolic abscess, and an abscess around a carcinomatous stricture of the large bowel has been known to track into the thigh. Viscera entirely surrounded by peritoneum may, after contracting adhesions, perforate into the retroperitoneal tissues and set up an abscess; this is most commonly seen in connection with the vermiform appendix, but it also occurs in disease of the female genital organs. Retroperitoneal suppuration may be set up by infection introduced at operations, *e.g.*, herniotomy. These abscesses may rupture into the bowel or into other hollow viscera, such as the bladder or vagina.

Clinical Picture.—The constitutional manifestations—fever, rigors, loss of flesh, rapid pulse, and leukocytosis—are more constant than the local. There is often abdominal pain or uneasiness, while some deep tenderness on pressure may be present, and in some cases a palpable tumor. Focal signs may, however, be absent, and the condition may be thought to be typhoid fever, generalized tuberculosis, or some obscure septicemia. In some instances a diagnosis of an abnormally situated appendicular abscess may appear the most probable.

Treatment is purely surgical.

SUBPHRENIC ABSCESS

Any abscess in contact with the under surface of the diaphragm, except when in the liver or in the spleen—the latter being rare—is

spoken of as a subphrenic abscess. From a clinical standpoint there are two forms of subphrenic abscess: (1) without any contained air—simple subphrenic abscess; and (2) containing gas—the subphrenic pyopneumothorax. Their aspects are so different that separate descriptions are necessary, but their anatomy is the same, the differences between them depending on the nature of the contents, and the same cause may, in different cases, give rise to either of these forms of abscess. Thus an appendicular subphrenic abscess, although generally simple, may contain gas, and an abscess due to gastric ulcer, although usually gaseous, is not so in all instances. Nothnagel states that about half the subphrenic abscesses contain gas. In 59 cases of subphrenic abscess at St. George's Hospital, tabulated by Wahby, 32 were gaseous and 27 non-gaseous.

Subphrenic Abscess without any Gaseous Contents.—Etiology.—The simple subdiaphragmatic abscesses which do not contain gas may in the first instance be due to pyogenetic infection derived from a solid abdominal viscus in the neighborhood of the diaphragm; but suppuration may track up from the vermiform appendix or from the pelvis, *e. g.*, from a pyosalpinx. A simple subphrenic abscess may in rare instances arise in connection with ulceration, simple or malignant, of the stomach or colon, but, as a rule, the resulting abscess in cases of perforating gastric ulcer contains air.

The causes of simple subphrenic abscesses may be conveniently tabulated in the order of their frequency:

1. Appendicitis is the most frequent cause and the resulting abscess is nearly always on the right side, but a left-sided abscess may follow. The formation of a subphrenic abscess is a grave complication or sequel of appendicitis; thus among 86 fatal cases of acute appendicitis, subphrenic abscess occurred in 7, or 8.13 per cent. (Christian and Lehr[1]). In some cases of subphrenic abscess the causal appendicitis may remain latent and be quite unsuspected. Appendicitis may give rise to a subphrenic abscess in several different ways. (*a*) An appendix which is retrocecal, or runs up behind and to the outer side of the ascending colon and over the right kidney, may almost touch the right lobe of the liver; an appendicular abscess in this position (*i. e.*, the right kidney-pouch) has a very short distance to travel to reach the under surface of the diaphragm. (*b*) An abscess around the appendix may spread upward in the paracolic groove to the right kidney-pouch and extend upward over the liver and under the diaphragm; this is the intraperitoneal route. The abscess may be retrocolic or retroperitoneal, and track upward. An appendicular abscess situated in the pelvis may extend upward along the paracolic grooves on both the right and the left sides of the abdomen, and so give rise to bilateral subphrenic abscesses. (*c*) A subphrenic abscess may be secondary to pylephlebitis set up by appendicitis; such a pylephlebitic abscess on the convexity of the liver may rupture and produce an abscess between the liver and diaphragm. (*d*) A residual abscess, the result of widespread peritonitis due to appendicitis, may form over the right lobe of the liver or around the spleen.

[1] *Medical News*, 1903, **82**, 147

2. Suppuration in the liver frequently sets up a non-gaseous subphrenic abscess. Collections of pus in the substance of the liver, such as tropical abscess, a suppurating hydatid cyst, multiple abscesses due to pylephlebitis or to cholangitis, whether associated with gall-stones or not, may by extension set up an abscess between the convexity of the organ and the diaphragm, or between the layers of the coronary ligament. Operations on the liver or bile ducts may give rise to leakage of infective material from inflamed areas in the liver. As rare causes of a subphrenic abscess, attention may be called to leakage of a tuberculous or of an actinomycotic abscess near the surface of the liver, or even of a softened and infected gumma in that situation.

3. An abscess of the spleen, by leaking or rupture, readily sets up a subphrenic abscess. Trauma, by giving rise to hemorrhage from or around the spleen, may be the first step in the production of a subphrenic abscess on the left side.

4. Although a localized abscess following perforation of a gastric ulcer nearly always contains gas, a very minute perforation, such as that produced by a pin, may set up a simple abscess. It is possible that microörganisms may pass through the floor of an ulcer, and that suppuration may occur without any gross perforation. Among 27 non-gaseous subphrenic abscesses at St. George's Hospital, 2 were associated with a non-perforated gastric ulcer. A non-gaseous abscess occurs in about 3 per cent. of all cases of gastric carcinoma, but the resulting abscess is usually not in actual contact with the diaphragm, and therefore rather comes within the category of perigastric abscess. The writer has seen a subphrenic abscess in connection with breaking down carcinomatous lymphatic glands close to the cardiac orifice of the stomach, the primary growth being in the lower end of the œsophagus.

5. Perforation of a duodenal ulcer usually floods the peritoneal cavity and sets up general peritonitis, but there are two ways in which it may set up a localized abscess (Maynard Smith[1]): (*a*) Perforation of the serous surface of the duodenum may be followed by the escape of a moderate amount of fluid into the right kidney pouch, and by the formation of an extensive abscess. (*b*) Perforation of the duodenum behind the peritoneum may give rise to a localized abscess. Osler estimates that 6 per cent. of subphrenic abscesses are due to duodenal ulcer. In his digest of 184 cases of duodenal ulcer, Cullen[2] finds that in 10 per cent. an abscess forms outside the duodenum, and that ultimately the ulcer opens into the abscess. In most exceptional instances a left-sided subphrenic abscess is due to a duodenal ulcer (Rolleston,[3] Box[4]).

6. A pericolic abscess may, but often does not, lie in contact with the diaphragm. Pericolic abscesses at the hepatic or splenic flexures of the colon will necessarily be those likely to become subphrenic.

7. Suppuration in or around the pancreas may spread so as to lie immediately under the diaphragm.

[1] *Lancet*, 1906, i, 895.
[2] *Scottish Med. and Surg. Jour.*, 1897, **1**, 643.
[3] *Brit. Med. Jour.*, 1912, i, 423.
[4] *Ibid.*, 1912, i, 889.

8. Suppuration in connection with the Fallopian tubes may, like an appendicular abscess in the pelvis, track up along the colon and give rise to a subphrenic abscess.

9. Retroperitoneal suppuration starting from the kidneys, and from tuberculous disease of the spine or even of the ribs, must be mentioned, since the abscess may be subphrenic, but the clinical picture is usually different from that of the other simple subphrenic abscesses.

10. It is sometimes stated that an empyema, other forms of intrathoracic suppuration, or even pneumonia, may lead to a subphrenic abscess. Tuberculous ostitis of the dorsal spine is commonly followed by a psoas abscess, but subphrenic abscess undoubtedly due to intrathoracic causes is extremely rare; in 448 collected cases there were 18 in which a subphrenic abscess was due to intrathoracic infection (Archibald[1]). In any given instance, therefore, it is more probable that the subphrenic abscess was the primary condition, but remained latent or was undetected for a time. Exploration of an empyema, however, may convey infection into the subphrenic space and so start an abscess below the diaphragm. In very rare cases suppuration in the posterior mediastinum, due to œsophageal ulceration, may track down and produce a subphrenic abscess. In a case of a tuberculous vomica in the lower lobe of the right lung, artificial pneumothorax performed for hemoptysis, and compression of the upper and middle lobes, a subphrenic abscess, communicating with the vomica and rupturing into the peritoneal cavity, was found (R. G. Hussey[2]). The infrequency with which infection spreads from the thorax to the abdomen is in marked contrast to the ease with which infection passes by the lymphatics from the peritoneum to the pleura. In 62 cases of streptococcic empyema, 14 spread from the abdomen (Pitt[3]).

11. In some instances the focus from which a subphrenic abscess arose cannot be found. Possibly a minute traumatic rupture of a solid organ allowing hemorrhage to occur, or perforation of some part of the alimentary tract by a small foreign body may be the real cause in some cases. Trauma may appear to be the only antecedent event.

Age and *Sex*. In 27 non-gaseous subphrenic abscesses at St. George's Hospital the average age was thirty-five years, being thirty-eight in 14 males and thirty-one in 13 females; in this series the incidence in the sexes was practically equal.

Morbid Anatomy.—Since a simple subphrenic abscess is in the majority of cases due to disease of the appendix or liver, it is much more often met with on the right than on the left side. It may be intraperitoneal or extraperitoneal, but is more commonly intraperitoneal. In 73 cases of subphrenic abscess due to appendicitis collected by Elsberg,[4] 35, or 48 per cent., were intraperitoneal; 20, or 27 per cent., extraperitoneal; and in 18, or 25 per cent., the position was not determined. Retroperitoneal abscesses due to lesions of the spine or kidney are more allied

[1] *Brit. Med. Jour.*, 1906, i, 1148.
[2] *Johns Hopkins Hosp. Rept.*, 1919, **18**, 86.
[3] *Clinical Journal*, London, 1907, **31**, 81.
[4] *Ann. Surg.*, 1901, **34**, 729.

to lumbar than to subphrenic abscesses. From a pathological point of view the greater cavity of the peritoneum is divisible into two parts: (*a*) Above the transverse mesocolon and omentum, supra-omental or supramesocolic; and (*b*) below the transverse mesocolon and omentum, or infra-omental. Intraperitoneal subphrenic abscesses occur in the supra-omental division of the greater sac. The anatomical boundaries of subphrenic abscesses vary according to the position of the abscess, and are further modified by the presence of old adhesions. The following descriptions may be regarded as applying both to simple and to gas-containing subphrenic abscesses.

The anatomical boundaries of subphrenic abscesses have been described by Box and Eccles,[1] and Carnot.[2] Barnard[3] described six forms of subphrenic abscess corresponding to six areas on the under surface of the diaphragm, four intraperitoneal and two extraperitoneal; the four intraperitoneal forms of subphrenic abscess are named (1) right anterior, (2) right posterior, (3) left anterior, and (4) left posterior; the areas on the diaphragm corresponding to these are defined and separated from each other by the cruciform arrangement of the peritoneal ligaments—the falciform, coronary, and right and left lateral—of the liver. The two extrahepatic subphrenic abscesses are (5) the right and (6) the left.

1. The right anterior subphrenic abscess is between the diaphragm and the convexity of the liver, and is bounded to the left by the falciform ligament, behind by the right lateral ligament of the liver, and in front by adhesions which vary somewhat in position; toward the right it communicates, unless shut off by adhesions, with the subhepatic or right kidney-pouch (Rutherford Morison), in which the right posterior intraperitoneal subphrenic abscess is situated.

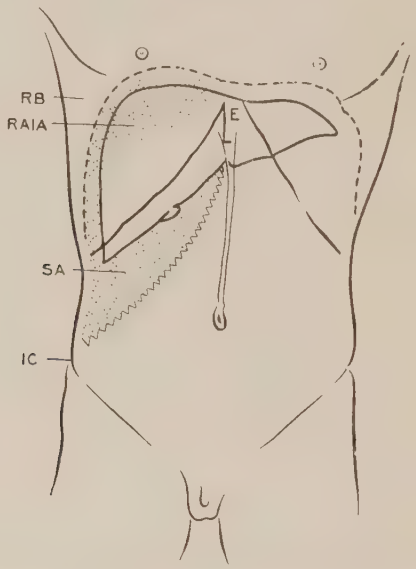
2. This right kidney-pouch may contain a pint of fluid before its contents run over into the remainder of the peritoneal cavity. Its boundaries are the right lobe of the liver above and in front, the hepatic flexure of the colon below, the parietal peritoneum of the lumbar region externally, the descending duodenum and lumbar spine internally, and the right kidney posteriorly. An abscess in this position commonly tracks up over the convexity of the liver into the right anterior subphrenic intraperitoneal space, and it may pass through the foramen of Winslow into the lesser sac of the peritoneum.

3. The left anterior intraperitoneal abscess (Barnard) is in the dome of the stomach chamber and is in relation with the stomach and the spleen, or perigastric and perisplenic, and occupies a pouch which corresponds to the right kidney-pouch (Box and Eccles) (Fig. 50). The phrenicocolic peritoneal ligament, binding the splenic flexure of the colon to the diaphragm and forming the suspensory ligament of the spleen, constitutes the lower margin of this pouch and, so to speak, dams up fluid in this peritoneal recess. The boundaries of left-sided intraperitoneal subphrenic abscesses are subject to some variation and Barnard's description is not followed here. Usually the abscess is between the left

[1] *Clinical Applied Anatomy*, 1906.
[2] *Sem. méd.*, Paris, 1906, **36**, 85.
[3] *Brit. Med. Jour.*, 1908, i, 371.

lobe of the liver, the diaphragm, the cardiac end of the stomach, and the spleen; the abscess passes deeply toward the back of the abdomen in relation to the spleen, and has the left kidney, adrenal, and tail of the pancreas behind. The spleen may lie in the middle of the abscess, and the abscess is often tortuous and irregular in outline as it passes around the margins of liver and spleen. In some cases the abscess is mainly to the left of the spleen, between it and the diaphragm; according to Hunt[1] this position of the abscess follows perforation of an ulcer on the posterior wall of the stomach. The abscess may also occupy the space between the diaphragm and the left lobe of the liver, passing

Fig. 49



The abdominal signs when a right anterior intraperitoneal subphrenic abscess (*RAIA*) is combined with a subhepatic abscess (*SA*) in the right kidney-pouch as often occurs in appendicular cases. The former (*RAIA*) produces signs of compression and inflammation at the base of the right lung (*RB*). The latter (*SA*) produces a triangular swelling below the liver margin, limited toward the abdomen by a band of tender rigid adhesions running from the ensiform cartilage (*E*) back into the right loin, usually as low as the iliac crest, *IC*. Pus or gas may be found in contact with the abdominal wall within the triangle. This and the two following figures are reproduced from Barnard's paper in the *Brit. Med. Jour.*, 1908, i, 371.

downward and to the right, under the liver, and in front of the stomach. Such an abscess is usually the result of suppuration in the left lobe of the liver or in connection with the anterior surface of the stomach.

4. An abscess confined to the lesser sac of the peritoneum is rare; it constitutes Barnard's left posterior intraperitoneal abscess.

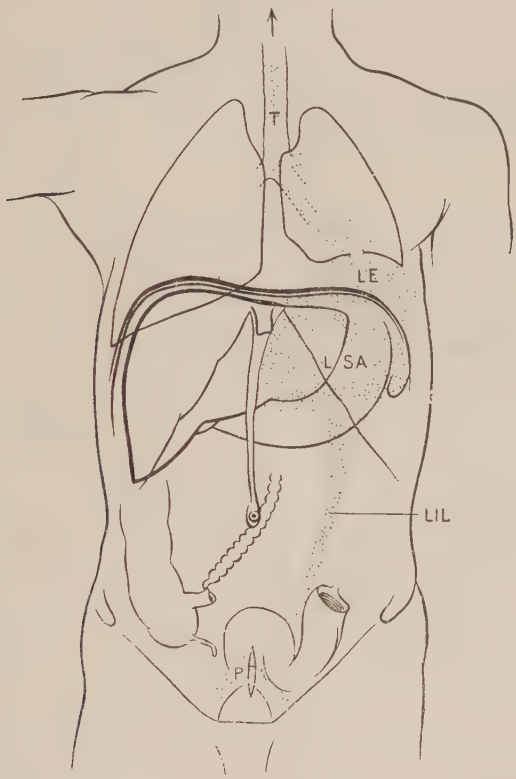
The median boundary of abscesses in contact with the under surface of the diaphragm is formed by the falciform ligament of the liver, which may be displaced by the pressure of the abscess, but is hardly ever perforated. It is extremely rare to find suppuration on both sides of

[1] *Trans. Med. Soc.*, London, 1905, **28**, 75.

the falciform ligament at the same time; but suppuration starting in the pelvis may track up in the paracolic grooves on both sides of the abdomen, and so give rise to abscesses in contact with the hepatic and splenic flexures of the colon.

5. The right extrahepatic abscess is in the uncovered space between the layers of the coronary ligament of the liver, and is closely allied to if not the same as the suprahepatic abscess described by Cantlie.[1] It is nearly always due to intrahepatic suppuration.

FIG. 50



Left anterior intraperitoneal subphrenic abscess (*LSA*) due to infection conveyed from pelvic appendicular abscess (*PA*) along (*LIL*) the left internal lumbar fossa (Barnard), or left internal paracolic groove (Jenkins and Maynard Smith). It has set up left-sided empyema (*LE*) which has burst into the trachea. (Barnard.)

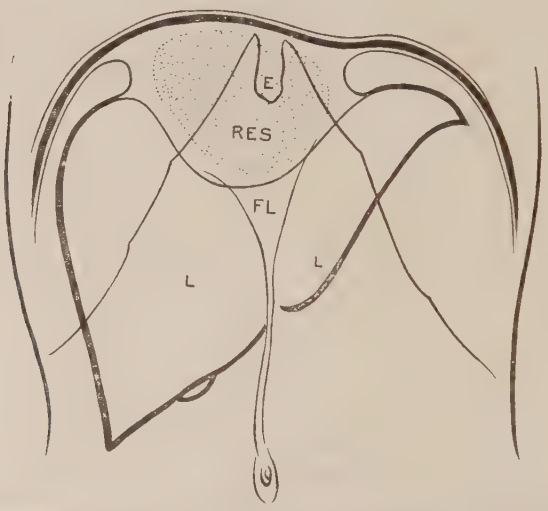
6. The left extraperitoneal abscess (Barnard) is near the left kidney and is rare. Barnard finds that the right anterior and left anterior intraperitoneal abscesses, due in the main to appendicitis and to perforated gastric ulcer respectively, are the commonest; next in order of frequency comes the right extraperitoneal abscess.

[1] *Brit. Med. Jour.*, 1899, ii, 646.

The walls of the abscess are formed of shaggy fibrin, the diaphragm, surface of the liver, intestines, and so forth, being infiltrated for a considerable distance with organizing granulation tissue. The size of the abscess varies very considerably in different cases; it may be as small as a man's fist or larger than a child's head, and contain several pints of pus. In cases of appendicular origin the pus is often putrid.

A subphrenic abscess readily sets up inflammation of the adjacent pleura and leads to an effusion which may be serous and sterile, fibrinous or purulent. This occurs in about half the cases of subphrenic abscess. Like an abscess in the liver, it may perforate the diaphragm and open into the pleura, leading to empyema, into the lung, thus setting up gangrenous pneumonia, multiple abscesses, and extensive disorganization of the lower lobe, or in very rare cases it may open into the pericardium. In Lang's[1] 173 cases of subphrenic abscess the diaphragm was perforated in 67, and in Martinet's[2] 138 cases in 33; both these series include gaseous

FIG. 51



The signs of a right extraperitoneal subphrenic abscess (*RES*) pointing in the epigastrium below the ensiform process (*E*) and having separated the layers of the falciform ligament (*FL*) so that the abscess may be opened extraperitoneally. The liver is pushed down. (Barnard.)

as well as non-gaseous abscesses. Intraperitoneal abscesses are less prone than extraperitoneal abscesses to perforate the diaphragm. The pus in the empyema may be extremely offensive; Dieulafoy[3] reported cases in which a non-gaseous subphrenic abscess of appendicular origin gave rise to a pyopneumothorax, the gas being due to bacterial activity and not to a communication with the lung or any of the hollow viscera. As the result of the rupture into the lung of a subphrenic abscess, set up by intrahepatic suppuration, a bronchobiliary fistula, with copious bile-

[1] *Thèse*, Moscow, 1895.
[2] *Thèse de Paris*, 1898.
[3] *Clinique médicale de l'Hôtel-Dieu de Paris*, 1901–1902, **4**, 105.

stained expectoration, may be established. Rupture externally or into the hollow viscera—the stomach or colon—is rare. Inflammation may extend to the portal vein and set up adhesive or, as a later stage, suppurative pylephlebitis. Rupture into the peritoneal cavity is usually fatal. It occurred once only among 23 cases of spontaneous rupture of a subphrenic abscess (Barnard).

Bacteriology.—The colon bacillus is commonly present; streptococci, staphylococci, pneumococci, *Bacillus pyocyaneus*, *B. typhosus*, actinomyces, and *Micrococcus melitensis* have also been found.

Symptoms.—These are somewhat obscure and vary to some extent according to the origin and the position of the abscess. Thus an abscess between the convexity of the liver and the diaphragm will resemble an intrahepatic abscess, while a purulent collection in the lesser sac of the peritoneum (bursa omentalis) will present features like those of a pancreatic cyst. In fact, subphrenic abscesses in these two positions are, from a clinical point of view, closely bound up with diseases of the liver and pancreas respectively.

The onset of symptoms is usually gradual, and it may be difficult to distinguish between those due to the primary disease, such as appendicitis or calculous cholangitis, and those depending on pus formation under the diaphragm. After an operation for an appendix abscess, continued fever, diarrhœa, and quick pulse may persist, and after some time signs at the base of the right lung suggest that an abscess has formed under the diaphragm. In some instances the thoracic manifestations, such as pleurisy, are the first to attract attention. This gradual onset contrasts with the sudden pain which marks perforation of the stomach in the majority of the cases of subphrenic pyopneumothorax. In some instances there is a sudden onset with a rigor.

Physical signs may be absent or so slight as to be easily overlooked, and are less obvious than in gaseous subphrenic abscess. From the point of view of physical signs, simple subphrenic abscesses have been divided into two groups: (1) those in which the thorax is mainly affected, and (2) those in which the signs are mainly abdominal.

1. Since a subphrenic abscess is usually nearer the spinal attachment of the diaphragm than the epigastrium, the signs are chiefly found posteriorly, and are more thoracic than abdominal. There is dulness at the base of one, usually the right, lung, which slowly increases upward toward the inferior angle of the scapula; there may be bronchial breathing from compression of the lung, a friction rub from concomitant pleurisy, or, from pleural effusion, absence of breath sounds. The physical signs, therefore, resemble those of pleural effusion. Examination with the *x*-rays may be of the greatest use by showing a dome-like elevation of the diaphragm on the affected side, and that its excursions are restricted or absent, but the presence of a pleuritic effusion vitiates this means of diagnosis.

2. In some cases, in which the manifestations are abdominal, a subphrenic abscess may pass forward, present anteriorly below the costal margin, and give rise to tenderness, fulness, and prominence of the hypochondrium and epigastrium, restricted movement of the ribs,

muscular resistance, and a more or less definitely palpable tumor, which is dull on percussion. The dulness is constant and does not alter when the patient's position is changed. Under an anesthetic the muscular rigidity passes off, and the intestine may pass in front of the abscess cavity and so lead to resonance where there was previously dulness on percussion (Godlee[1]). As the abscess approaches the surface the skin may become œdematous and red, and fluctuation may be obtained. The manipulation necessary to elicit this sign is, however, not without risk of producing rupture into the general peritoneal cavity. Pain is usually not a severe symptom, and, as a rule, is pleuritic and transient; it may be felt at the angle of the scapula. The temperature is nearly always raised and may show the oscillations of suppuration, but in a few instances fever is absent. The pulse is quick, the respirations are often irregular, painful, and rapid, especially when the thorax is much invaded; cough is exceptional. Leukocytosis up to 30,000 may be present. The appetite is poor, wasting is considerable, and there may be frequent perspirations, especially at night, and considerable secondary anemia. When clubbing of the fingers occurs in a case thought to be one of subphrenic abscess the lesion will probably turn out to be above the diaphragm (Acland[2]). With continued temperature and progressive loss of strength the patient steadily goes down hill unless the abscess be freely drained. The abscess may extend and open into the pleura, lung, bronchus, into the peritoneum, one of the abdominal viscera, or even externally through the ribs or at the umbilicus. In exceptional instances the abscess has burst into the pericardium, or has tracked up into the neck (Cullen). Pulmonary embolism may result from thrombosis of branches of the inferior vena cava. Death usually results from exhaustion. The duration of the disease, if it be left to run its natural course, is from two to three months.

Diagnosis.—When there is no antecedent condition, such as appendicitis or suppuration elsewhere in the abdomen, the existence of a subphrenic abscess may not be suspected unless there be a palpable swelling. On the other hand, when after operation on an appendix abscess or on the gall-bladder or biliary passages, the patient's general condition still suggests suppuration, careful examination of the bases of the lungs by percussion, auscultation, and the roentgen-rays may show signs compatible with a small abscess or effusion. The affected area should then, as Barnard directs, be systematically explored with a syringe, the needle of which is at least three inches long and sufficiently large to enable thick pus to be withdrawn. The patient is fully prepared for operation and anesthetized, and the needle is passed deeply—for three inches—into the 10th intercostal space in the scapular line, and then, if no pus be found, into the 9th, 8th, 7th, and 6th spaces in turn; if necessary, the same spaces in the midaxillary line are explored from below upward. When a subphrenic abscess presents under the anterior abdominal wall the exploring syringe should not be used.

[1] *Lancet*, 1905, i, 482.
[2] *System of Medicine* (Allbutt and Rolleston), 1907, 3, 1007.

Differential Diagnosis.—The chief difficulty in distinguishing between subphrenic abscess and other intra-abdominal conditions on the right side is in deciding whether the collection of pus is inside the right lobe of the liver or between it and the diaphragm. Enlargement of the liver downward is in favor of intrahepatic suppuration, but in many instances it is impossible to come to a positive conclusion, and, indeed, a subphrenic abscess is often due to leakage of an intrahepatic focus of suppuration. A subphrenic abscess on the left side presenting as a palpable swelling must be distinguished from soft tumors, innocent, such as perirenal lipomas, or malignant, such as retroperitoneal sarcomas. The raised temperature and signs of septic absorption should be taken into account in forming an opinion, but a swelling in the left hypochondrium of rather sudden onset, accompanied by pain and a raised temperature, has turned out to be a retroperitoneal sarcoma. In some instances a large, false abdominal aneurism on the left side does not pulsate and no bruit is audible over it; the diagnosis may then be very difficult (T. Holmes[1]). Persistent leukocytosis is in favor of abscess, but a posthemorrhagic leukocytosis may occur in aneurism.

The main difficulty, however, is not in distinguishing between subphrenic abscess and other abdominal conditions, but between subphrenic abscess on the one hand and an empyema or pleural effusion on the other. It has happened that when an abscess diagnosed as an empyema is drained, particles of food are found in the discharge, and for the first time indicate the underlying cause. In a simple subphrenic abscess on the right side the liver is more depressed, the breath sounds less cut off at the base of the lung behind, and the constitutional symptoms are more marked in comparison with the thoracic dulness than in an empyema. Skiagraphy shows that the diaphragm is pushed up instead of being depressed.

The question whether the collection is above or below the diaphragm is often rendered more difficult by the not infrequent presence of a pleural effusion secondary to the suppurative process under the diaphragm. When a pleural effusion and a subphrenic abscess are both present the latter is extremely likely to be overlooked. This combination, if suspected, may be recognized by the withdrawal by the exploring syringe of pus from one interspace and serous fluid from one above it. This sign, however, is not infallible, for in rare cases a loculated pleural effusion may contain serum in one loculus and pus in another.

Brief reference may be made to two signs which have been employed in order to decide whether a given collection of fluid is above or below the diaphragm. If the aspirating needle is introduced into a cavity above the diaphragm no movement of the needle occurs on respiration; if the needle passes through the diaphragm the extrathoracic part of of the needle moves upward in inspiration and downward in expiration; this is Fürbringer's sign. The second sign is Pfühl's; when the needle enters a subphrenic abscess the manometric pressure and the outflow of pus are greater during inspiration and less during expiration, while

[1] *St. George's Hospital Reports*, 1875, **7**, 173.

the reverse holds good in the case of an empyema. These two signs depend on the normal excursions of the diaphragm being maintained, but this does not always hold good; for example, a pleural effusion may paralyze the diaphragm and so lead to mimicry of the condition in a subphrenic abscess. Further puncture of the diaphragm may convey infection from the abdomen to the thorax, or *vice versa*, and is therefore not devoid of danger.

Prognosis in non-gaseous subphrenic abscess depends on the condition being recognized and promptly treated by exploration and thorough drainage. If the abscess be not opened the case will almost certainly terminate fatally; further, it is most important that the abscess should be opened before it has extended into the lung or given rise to septicemia. Even when opened there is a risk that some loculus of the abscess may not drain properly. The difficulty in diagnosing and, when the existence of the abscess is suspected, in accurately locating the abscess makes the prognosis grave. A subphrenic abscess may be opened successfully, but an empyema may be overlooked and prove fatal.

Most of the available statistics contain both simple and gas-containing abscesses, so that it is difficult to compare the mortality of the two forms. In Elsberg's 73 cases of subphrenic abscess (15 per cent. of which were gaseous) due to appendicitis, 51 were operated upon, with recovery in 40, or 78.4 per cent., while of 22 not operated upon 18, or 82 per cent. died. Out of Barnard's 76 cases, 36, or 47.4 per cent., died; 12 cases were only recognized after death and were not operated upon. Of the remaining 64 the mortality was 37.5 per cent., but after making allowance for imperfect diagnosis and treatment, Barnard concluded that the mortality should be 16 per cent.

Treatment is purely surgical.

Subphrenic Pyopneumothorax.—The peculiarity of this form of subphrenic abscess is that at the bedside it imitates an ordinary pneumothorax or pyopneumothorax. The existence of a gaseous abscess underneath the diaphragm was first diagnosed during life as a logical deduction from the physical signs by G. H. Barlow[1] as far back as 1845, but it was not until Leyden's[2] article, in 1880, that it became generally recognized and the subject of numerous papers. Since perforated gastric ulcers have been treated by immediate operation this form of subphrenic abscess has become less common.

Etiology.—The causes of a gaseous subphrenic abscess are less numerous than those of a simple subphrenic abscess. Perforation of a gastric ulcer is the most important cause. In the sixty years, 1846 to 1906, there were about 26,000 autopsies at St. George's Hospital, among which Wahby found 32 gaseous subphrenic abscesses, 25 (21 females, 4 males) of which, or 78.1 per cent., were due to perforated gastric ulcer. In order that the resulting peritonitis should be localized, certain conditions are necessary; thus preëxisting adhesions which prevent the gastric contents from spreading widely over the peritoneum are of great importance. It is, however, highly probable that in certain circumstances

[1] *London Medical Gazette*, 1845, **1**, 13.
[2] *Zeit. f. klin. Med.*, 1880, **1**, 320.

perforation of the stomach may lead to a localized abscess even in the absence of these adhesions; the occurrence of perforation in a stomach containing but little food, in a patient in the supine position, so that only a small quantity of the gastric contents escapes and does not travel far into the peritoneal cavity, and then mainly into the upper part, gives a combination of circumstances in which the inflammatory process may become circumscribed instead of generalized. The position of the perforation is another factor of importance: if on the posterior surface, a localized abscess is likely to follow, while if it is on the anterior surface, general infection of the peritoneum is apt to occur. Perforation of an ulcer close to the pylorus may lead to a localized abscess in the right kidney-pouch. Perforation of the stomach due to carcinoma is a rare cause of a gaseous abscess.

Perforation of a duodenal ulcer usually gives rise to general peritonitis, but in a small minority of the cases a subphrenic pyopneumothorax on the right side results. Out of 32 gaseous subphrenic abscesses at St. George's Hospital, 6 (3 males, 3 females), or 19 per cent., were due to perforation of a duodenal ulcer.

An abscess in the neighborhood of the stomach or duodenum has in rare instances perforated (exogenous ulceration) into the alimentary canal, with the result that a gaseous subphrenic abscess is produced. A suppurating hydatid cyst of the liver may rupture into the alimentary canal and become gaseous, but this condition, of which Dévé[1] has collected 7 examples, is not the same as an ordinary subphrenic pyopneumothorax. A suppurating hydatid of the liver, from infection with anaërobic organisms, may contain gas, and in rare instances, by rupturing into the space between the liver and the diaphragm, may produce a subphrenic pyopneumothorax on the right or left side, according to the position of the cyst in the right or left lobe of the liver. In Maydl's[2] collection of 179 cases of subphrenic abscess there were 3 of gaseous subphrenic abscess due to hydatid cysts of the liver. Perforation of an ulcer in the colon very seldom produces a gaseous abscess.

An appendicular abscess, although usually simple, may be gaseous; this was so in 15 per cent. of the 73 cases of subphrenic abscess due to appendicular infection analyzed by Elsberg.[3] The presence of gas in these abscesses was at first considered to be due to secondary communication with some air-containing viscus, but it is, in many instances at least, of bacterial origin.

Morbid Anatomy.—The situation and boundaries of subphrenic abscesses have been described. In contrast to simple subphrenic abscesses, which are much commoner on the right side, gas-containing subphrenic abscesses are in the great majority of cases on the left side. This is due to the preponderating influence of perforated gastric ulcers as the causal factor.

The diaphragm is pushed up so as greatly to encroach on the cavity of the thorax. The perforation in the stomach or duodenum is usually

[1] *Rev. de chir.*, Paris, 1907, **35**, 529.
[2] *Ueber subphrenische Abscesse*, 1894, Wien.
[3] *Ann. Surg.*, 1901, **34**, 729.

open, but in some instances becomes closed with fibrin. The size of the cavity may vary considerably; sometimes these abscesses are very large, and have been known to contain in addition to gas a quart of purulent fluid with an admixture of gastric contents of an extremely offensive character. The abscess may erode the substance of the spleen. Perforation into the general cavity of the peritoneum occurs in a few cases. The inflammatory process readily spreads through the diaphragm and sets up pleurisy with effusion and collapse of the lower lobe of the lung. The effusion is usually serous or serofibrinous, but may be purulent, and in this even the lung may be disorganized by multiple abscesses. Perforation of the diaphragm may be followed by a true pyopneumothorax or, when the lower lobe of the lung is already adherent to the diaphragm, by suppurative destruction of the lung or gangrenous pneumonia; or the abscess may rupture into the bronchi. Pericarditis may be found, but is not so frequent as pericardial friction during life.

Age and *Sex.*—As most cases are due to perforation of a gastric ulcer, the patients are chiefly young women. In the 32 cases at St. George's Hospital the average age was thirty-three years, being thirty years in the 24 females and forty-two years in the 8 males. Vanlair recorded a gaseous subphrenic abscess in a boy six years of age.

Symptoms.—The onset is usually sudden, with very severe pain, due to perforation of the stomach; in this respect it differs from the simple subphrenic abscesses in which the onset is often insidious. In some cases, however, the leakage from the stomach is quite latent. The patient's history often shows indications of gastric ulcer. The pain, which is agonizing and may be accompanied by collapse, is situated in the upper part of the abdomen, usually on the left side. The onset may be accompanied by vomiting, which may or may not persist afterward; the vomited matters may contain blood and bile. It is important to realize that vomiting may occur after perforation of a gastric ulcer, and that this event does not seriously militate against that accident. Directly after the onset the abdomen becomes extremely tender, so that accurate examination may be impossible at first; as a rule, it rapidly becomes distended, although in men it may be rigidly contracted, tympanitic, and does not move on respiration. The temperature becomes raised, the pulse and respiration rates are rapid, rigors may occur, leukocytosis is present, there is nocturnal sweating, and the patient has the general appearance of suppuration with abdominal pain and some respiratory embarrassment.

The *physical signs* may very closely resemble those of a true pneumothorax or pyopneumothorax. There is a tympanitic note on percussion over an area of distention in the upper part of the abdomen; the altered note extends up into the thorax for a considerable distance, but not to the extreme apex. On the right side the diaphragm may be displaced as high as the second rib, but the presence of the heart prevents the same amount of upward displacement on the left side. The tympanitic note may be mainly behind the sternum. There is dulness posteriorly on the affected side when the patient is lying on his back, and when turned on his side the positions of the dull and tympanitic areas alter

as in a pyopneumothorax. A bell or coin percussion note, amphoric breathing, succussion, and metallic tinkling may be heard over the swelling and part of the chest. When the left side is affected the heart is displaced upward, but only slightly to the other side, thus differing from what occurs in a true pneumothorax. When the abscess is on the right side the liver may be greatly displaced downward and be palpable below the umbilicus; the hepatic dulness will then be absent from its normal position. The costal margin is pushed out and the lower intercostal spaces may bulge as in pneumothorax.

Thoracic complications are almost constant. Signs of pleurisy rapidly come on, but in some instances the signs are those of pneumonia of the base of the lung on the corresponding side. The effusion is usually serous at first, but may subsequently become purulent. A pleuropericardial or pericardial friction rub is not uncommon. Secondary parotitis occasionally occurs, and if suppuration supervenes may prove very serious. In rare instances subcutaneous emphysema has appeared.

Diagnosis.—The common error is to regard as a pyopneumothorax a gaseous abscess which is below the diaphragm. While the history and mode of onset frequently point to the abdomen rather than to the thorax, the signs suggest a pyopneumothorax from which it can be most certainly distinguished by a skiagram showing the position of the diaphragm.

The physical signs in favor of a gaseous subphrenic abscess are that the pneumothorax appears to be partial, not universal, as shown by the presence of normal breathing over the upper part and apex of the lung; that the heart's apex is displaced upward and but little to the opposite side; that a bell note and other signs of an air-containing cavity can be obtained well below the limits of the thoracic cavity, for example, below the left costal margin; and that cough and expectoration are late in appearing, or insignificant.

A subphrenic pyopneumothorax is often complicated by a pleural effusion—serous or purulent; the diagnosis of these two concomitant conditions may be greatly aided by the withdrawal of pus and gas from one interspace, and of serum or pus of a different character from a higher interspace. The fluid from a subphrenic abscess comes out more freely during inspiration, while in a pleural effusion its exit is accelerated during expiration. It must be remembered, however, that puncture of the chest, although often desirable to determine whether, and if so where, operative procedures should be carried out, may spread infection from the pleura to the peritoneum or *vice versa*.

The diagnosis from a pleural effusion rests on the detection of the signs of a cavity containing fluid and gas, on the changing dulness in a gaseous subphrenic abscess, and on the absence of this change in a pleural effusion (Godlee), on the lateral displacement of the heart in a pleural effusion, and upon its upward displacement in a subphrenic gaseous abscess.

Abdominal distention due to flatulence may be accompanied by disappearance of the normal liver dulness and by a bell note, but the liver cannot be felt to be displaced downward.

A diaphragmatic hernia on the left side which contains the stomach gives rise to signs resembling in many respects those of a pyopneumothorax, but the abdomen falls in instead of being distended, and the heart is pushed over to the right side very much more than in a subphrenic pyopneumothorax. In making a diagnosis the *x*-rays should be employed, and a metal probe passed into the stomach and its position noted.

Prognosis.—In subphrenic pyopneumothorax this is always grave, partly because the extension of inflammation to the pleura and lung is a frequent and serious complication, and partly because the large abscess cavity may not close and the patient dies from toxic absorption.

Treatment is surgical, and consists in opening and draining the abscess.

SIMPLE CHRONIC PERITONITIS

This condition may for convenience be divided into (1) circumscribed or localized areas of chronic peritonitis, and (2) diffuse chronic peritonitis. There are necessarily transitional cases in which the chronic peritoneal change is, on the one hand, not sufficiently localized to be included in the first category, and, on the other hand, is far from implicating the whole of the peritoneal cavity. As a matter of fact, chronic peritonitis is seldom universal and equally well-marked over the entire abdominal cavity. The change may be advanced in the upper part of the abdomen over the liver, spleen, and omentum, and slight in the pelvis.

Localized Chronic Peritonitis.—The adhesions due to a past acute peritonitis must be distinguished from the progressive or chronic inflammatory process which alone deserves the name of chronic peritonitis.

The causes of localized chronic peritonitis are numerous. The female genital organs very commonly give rise to chronic pelvic peritonitis which produces dense adhesions around the Fallopian tubes, ovaries, and uterus. The vermiform appendix and the broad ligament may become so matted together that even after death it is extremely difficult to determine in which of these structures the inflammatory process originated. The main cases of chronic perimetritis and pelvic peritonitis are gonococcic and puerperal infections. It is highly probable that hemorrhages from the Fallopian tubes may, as the result of subsequent microbic activity, be responsible for chronic pelvic peritonitis. A chronic gastric or duodenal ulcer may produce progressive localized peritonitis in the immediate vicinity. The contraction of the thickened peritoneum may play a part in producing hour-glass contraction of the stomach, duodenal stenosis, or even stricture of the common bile duct. Appendicitis is an important cause of localized chronic peritonitis in the right iliac fossa. Chronic peritonitis may also be limited to the orifice of hernial sacs, to the surface of the intestines in chronic intussusception, be part of diverticulitis, and may form prominent masses over the sigmoid colon or cecum in schistosomiasis (H. E. Drew[1]). Foreign body tubercles due to the escape of particles of oat-seed were found by Shennan[2] in the visceral peritoneum of the right upper quadrant of the abdomen, chiefly

[1] *Jour. Path. and Bacteriol.*, Edin., 1923, **26**, 27.
[2] *Ibid.*, 1923, **26**, 82.

over the pylorus. Instruments left in the peritoneal cavity after operation, of which Crossen[1] collected 50 cases in 1909, and Clifford White[2] published 44 unrecorded examples in 1923, may set up various results, adhesions especially by the protective action of the omentum, peritonitis or abscess from ulceration of the adjacent viscera. Chronic cholecystitis, especially when associated with gall-stones, may set up very marked local peritonitis which unites the gall-bladder to the neighboring viscera, especially the pylorus.

In hydatid or other cysts, such as ovarian, there may be such thickening of the overlying peritoneum that the condition resembles a lamellar or corneal fibroma. As the result of friction or pressure, chronic capsulitis of the spleen and liver may occur. Localized thickenings, white in color, raised above the surface of the capsule of the spleen, are common in splenomegaly; they are composed of dense white fibrous tissue and are spoken of as lamellar or corneal fibromas. Much less commonly similar masses are found on the surface of the liver.

Clinically, the results of localized chronic peritonitis are variable. The lamellar fibromas of the spleen do not give rise to symptoms. Adhesions and indurations around the stomach and flexures of the colon and elsewhere may interfere with the natural movements of the viscera. Thus in the case of the stomach there may be persistent pain after food, or "adhesion dyspepsia;" this is not uncommon in women formerly the subjects of gastric ulcer, and may be thought to be due to a relapse of that disease. As a very rare result of perigastric chronic peritonitis there may be compression of the common bile duct and jaundice. In one example of this, secondary to a chronic ulcer near the pylorus, there was such extensive fibrosis that a tumor, regarded as malignant during life, could be felt. Chronic peritonitis around the gall-bladder may lead to pyloric obstruction and dilatation of the stomach.

Chronic peritonitis around the colon, especially the flexures, may give rise to constipation and pain, especially after defecation; according to the position of the lesion, the condition may imitate appendicitis or malignant disease of the colon. The peritoneal bands in connection with the ascending and transverse colon described by Lane, as the result of intestinal stasis and due to "crystallization of lines of strain" and by Jackson as due to membranous pericolitis, are by others regarded as congenital and not pathological in origin.

Patients vary much in the way in which they feel such pain; some are martyrs to these painful peritoneal adhesions, while in others—probably in the great majority—there is little or no inconvenience. The adhesions may produce acute intestinal obstruction by kinking and strangulation of the intestine. In some instances the persistent pain suggesting chronic appendicitis may justify laparotomy. Short of this, the treatment should be directed to diet, prevention of constipation, local measures for the relief of pain, and to improvement of the general health.

Chronic peritonitis involving the sigmoid mesocolon (perimesosigmoiditis) and the mesentery of the lower part of the ileum (chronic mesenteric

[1] *Am. Jour. Obst.*, 1909, **59**, 58, 250.
[2] *Brit. Med. Jour.*, 1923, i, 228.

peritonitis) was described by Riedel as the result of constipation. But Küss[1] has insisted on the spread of infection from the pelvic organs, especially of females in whom the condition is much commoner than in males, and on the production of stenosis of the sigmoid and rectum by the cicatrizing pericolitis. There is a radiating thickening of the mesocolon which has been regarded as an important factor in the production of volvulus of the sigmoid flexure. The symptoms of pericolitic stenosis of the sigmoid and rectum are those of carcinomatous stricture. In one case the dense fibrosis, due to salpingitis, so compressed the ureters as to cause fatal uremia.

Diffuse Chronic Peritonitis.—Under this heading it is convenient to consider cases which have in common a diffuse peritoneal inflammation of chronic and progressive character, not manifestly due to tuberculosis or new growth. It is sometimes called simple chronic peritonitis to distinguish it from the two forms just mentioned. Chronic proliferative and chronic indurative peritonitis are synonyms sometimes employed, and since ascites is extremely common, the name chronic exudative peritonitis is almost as applicable.

Etiology.—There is considerable difference of opinion as to the relative importance of the causal factors. The classification of chronic peritonitis here adopted is: (1) When associated with varying degrees of chronic inflammation of the pericardium and pleuræ. (2) When associated with arteriosclerosis and granular kidneys. (3) When associated with other conditions. The first two categories are the most important.

1. Simple chronic peritonitis may be combined with inflammatory changes in the pericardium and pleuræ. The association of similar inflammatory changes, whether acute or chronic, in two or more serous cavities has been called polyserositis and polyorrhomenitis. When the condition is chronic it has also been termed multiple progressive hyaloserositis or Concato's disease. The chronic inflammatory changes in the thorax that may be found in association with simple chronic peritonitis vary in extent and intensity; thus there may be chronic indurative mediastinopericarditis with obliteration of both pleuræ, chronic mediastinitis alone, or adherent pericardium. Cases associated with adherent pericardium are the most usual. In some cases of long standing the thickened and adherent pericardium may be calcified; the peritoneal change is then advanced and the liver may be cirrhotic, thus differing from its usual condition of that organ—chronic venous engorgement and fatty change—in chronic peritonitis. It is generally considered that when chronic intrathoracic and peritoneal serositis are associated, the primary focus is more often intrathoracic; but infection spreads more rapidly from the abdomen to the thorax than *vice versa*.

The original starting-point of the inflammation may thus be on either the upper or under surface of the diaphragm; when there is an adherent pericardium, especially if it be calcified, it is probable that the original focus was in this position. The original lesion may be an acute pericarditis or perihepatitis, or there may be recurrent attacks. But on whichever

[1] *Rev. de chir.*, Par., 1910, **41**, 190, 503, 688.

side it starts it spreads through the diaphragm, the constant movements of which interfere with the natural cure of the morbid process, and so induce the chronic inflammatory process which is most marked on each side of the diaphragm and fades off in the more distant parts of the adjacent serous membranes. The chronic peritonitis is, therefore, most advanced over the liver and spleen.

The pericardial pseudocirrhosis described by Pick[1] is probably allied to this form of chronic peritonitis; Pick, however, believed that a latent adherent pericardium gives rise to circulatory disturbance in the liver, hepatic fibrosis, ascites, and that chronic peritonitis, although it might result from the ascites and repeated tappings, was a more or less accidental and secondary event. Nicholls[2] and Kelly[3] specially associated chronic peritonitis with similar intrathoracic changes.

2. The association with arteriosclerosis and granular (arteriosclerotic) kidneys was insisted on by Hale White,[4] who found it in 19 out of 22 cases of universal perihepatitis and peritonitis, but some observers do not attach much importance to its etiological influence.

3. Syphilis appears from the frequency of a positive Wassermann reaction to be a cause of simple chronic peritonitis (Letulle[5]). Smit[6] points out that hour-glass contraction of the stomach may be a result of the fibrous form of chronic syphilitic peritonitis and Korach[7] considers that indurative peritonitis, especially around the appendix which is healthy, may be syphilitic in origin. In late congenital syphilis it may spread by extension from the viscera (Acuña and Casaubon[8]).

4. Simple chronic peritonitis may occur in combination with various intra-abdominal lesions, or its starting-point may be quite obscure. The associated lesion, such as syphilis of the liver, may reduce the resistance of the peritoneum, or, as in the case of chronic duodenal ulcer or cholecystitis, may provide a local focus for infection. In such cases a widespread chronic inflammatory process results instead of the local reaction which would be expected; this may be compared with the formation of large cheloids after minute injuries, and possibly the excessive reaction may depend on a low resistance, inherent or acquired, of the peritoneum in that individual.

Alcoholism by reducing the resistance of the peritoneum and by setting up gastro-intestinal inflammation would favor infection. The chronic venous engorgement due to heart and other obstructive diseases would act in much the same manner. The relation of ascites to the chronic peritonitis is usually considered to be that the chronic peritonitis causes the ascites, but in some circumstances the reverse may hold good; thus, in chronic ascites due to backward pressure of heart disease, repeated tappings may favor a low form of infection, which is not necessarily introduced from without but may be carried by the blood stream. In some cases trauma appears to be the exciting factor, and that by damag-

1 *Ztschr. f. klin. Med.*, 1896, **29**, 385.
2 *Studies from the Royal Victoria Hospital*, Montreal, 1902, i, No. 3.
3 *Am. Jour. Med. Sci.*, 1903, **125**, 116.
4 *Trans. Clin. Soc.*, London, 1888, **21**, 219.
5 *Presse méd.*, Par., 1918, **26**, 477.
6 *Nederl. Tijdschr. v. Geneesk.*, 1924, **58**, 899.
7 *Deutsch. med. Wchnschr.*, 1924, **50**, 1402.
8 *Arch. méd. des enf.*, Paris, 1922, **25**, 157.

ing the viscera it would allow of a low form of infection of the peritoneum. Lastly, no obvious cause may be forthcoming.

Pathogeny.—Since the process is evidently a chronic and progressive form of inflammation, it has been ascribed to infection with microörganisms of a low grade of virulence. The *Bacillus tuberculosis*, *Bacillus coli*, *Bacillus typhosus*, and the pneumococcus have been suggested. Louis (1825) regarded chronic peritonitis as always tuberculous; Picchini (1891) argued that subacute and chronic polyorrhomenitis is practically always tuberculous. The recognition of a special form of tuberculosis, the chronic hyperplastic, which is best known in connection with the ileocecal part of the intestine, suggests that there may be a chronic hyperplastic tuberculous peritonitis which bears the same relation to ordinary tuberculous peritonitis that chronic hyperplastic tuberculosis of the intestine does to ordinary intestinal tuberculosis. It may be pointed out that tubercle bacilli are found in some cases of ascites which do not otherwise suggest peritoneal tuberculosis, and that tuberculosis with fibrotic changes is a not uncommon complication of arteriosclerosis. The last point may help to explain the association of arteriosclerosis and granular kidney with simple chronic peritonitis.

Morbid Anatomy.—The appearances vary considerably from the more marked changes of the "iced" organs to a general slight opacity of the peritoneum. In a well-marked case the peritoneum is covered by a thick membrane which resembles a thin layer of cartilage; it is dull white or glistening and pearly in color, and may show pigmentation. This dense layer, especially over solid organs, such as the liver and spleen, for which it forms a firm casing, may show a few depressions like the pitting of sand by rain drops. It is possible that these deficiencies are the result of rupture of the dense fibrous tissue induced by its own contraction. On the other hand the thick membrane may be locally accentuated in the form of fibrous elevations or nodules, perhaps more often seen on the parietal peritoneum; to this condition the name "peritonitis fibrosa" has been applied; these fibrotic elevations when small may closely resemble miliary tubercles, or when large, nodules of disseminated malignant disease.

The thick membrane, which may be even one-quarter of an inch in depth, can usually be peeled off the liver and spleen, leaving their capsules in a fairly normal condition. From its marked tendency to cicatricial contraction it squeezes the organs and leads to atrophy; in extreme instances these organs may therefore become so atrophied as to be isolated in the abdominal cavity and lose their normal relations. The omentum becomes shortened and rolled up into a firm cord, often in irregular knots, running transversely across the abdomen; in some instances hardly a trace of the omentum is left. In like manner the mesentery becomes retracted, so that the small intestines are anchored to the spine and cannot float in the ascitic fluid, "and, if a hernia has existed, it will sometimes be found to have been completely reduced" (Hodgkin[1]). At the same time there may be great diminution in both

[1] *Lectures on the Morbid Anatomy of the Serous and Mucous Membranes*, London, 1836, **1**, 152.

the length and diameter of the alimentary canal. In extremely rare cases the valvulæ conniventes become so closely packed that the longitudinal section of the intestine may resemble a comb and death from intestinal obstruction may result (Porter and Welch;[1] Dowd[2]). Intestinal obstruction is, however, more likely to be due to the numerous kinks produced in the intestine. The colon may be no larger than the small intestine. This gives rise to impaired absorption. The condition has been called "peritonitis deformans." Subacute or acute peritonitis may supervene.

Adhesions are often present, but their extent varies greatly. They are more often seen over the solid and relatively fixed organs, since the peristalsis of the intestines interferes with their formation and may rupture them when formed. A thick membrane may cover over the intestines, especially in the ileocecal region. The remains of adhesions may be seen as filamentous or villous tags on the small intestine, and sometimes resemble miliary tubercles. Adhesions are not uncommon between the liver or spleen and the diaphragm, and may be dense or delicate. Acute strangulation of the intestine due to bands is very rare in this form of chronic peritonitis. When there are sufficient adhesions the ascitic fluid may become encysted, and when the adhesions are so numerous as to obliterate a large area of the peritoneal cavity the fluid effusion may be slight.

The liver and spleen are often described as "iced," or as showing universal chronic capsulitis, and in the case of the liver as "*Zuckergussleber*" (Curschmann). This condition, also called universal chronic perihepatitis, was formerly regarded as a distinct morbid entity, and many cases of chronic ascites, in reality due to chronic peritonitis, were regarded as the result of chronic perihepatitis, the existence of the more widespread peritoneal change being ignored or regarded as a secondary result of the recurrent ascites and consequent tappings. From the frequency of ascites in hepatic cirrhosis the liver was considered the important factor in the production of ascites, and disease of its capsule was therefore accepted as a sufficient cause of ascites without any reference to the peritoneal change. The thickness of the membrane varies in different parts; it modifies the shape of the viscera, rounds off the edges, and covers up natural depressions. The gall-bladder may be almost buried, and is usually collapsed, but constriction of the bile duct or portal vein is very rare. In a case at one time under my care prevertebral chronic peritonitis leading to obstruction of the lymphatics and so to elephantiasis was found at the autopsy.[3] The organs usually show chronic venous engorgement, but any considerable extension of fibrosis from the capsule into the substance of the organs is very rare.

Microscopically there is extremely dense fibrous tissue laid down in parallel lamellæ, with a few nuclei between. The fibrous tissue is prone to undergo hyaline change, hence the condition has been called hyaloserositis (Nicholls). The deeper layers of the membrane show bloodvessels with collections of leukocytes and mast cells. Nicholls was unable to

[1] *Jour. Am. Med. Assn.*, 1908, **50**, 719.
[2] *Ann. Surg.*, 1923, **77**, 423.
[3] *Brit. Med. Jour.*, 1907, i, 617.

find any evidence of fibrin. As the wrinkled peritoneum can be seen underneath, the formation of the membrane is due to organization of exudation, and not to hyperplasia of the peritoneum.

Clinical Picture.—The condition most commonly occurs in middle life, but it may be seen in children; the sex incidence is about equal.

The cases may present different manifestations, but the characteristic result is chronic ascites, which requires numerous tappings and recurs with remarkable persistence. The interval between successive tappings may diminish in progressive cases so that paracentesis may become necessary every week; more than 100 tappings may be required. After tapping, the rolled up omentum may be clearly felt running across the abdomen, and is often more distinctly palpable toward the left hypochondrium. The other signs of ascites will be found. The distended abdomen may be almost uniformly dull, since from retraction of the mesentery the small intestines are tethered to the spine and unable to reach the abdominal wall. In rare instances friction is audible. In some cases the fluid is encysted and the abdomen is irregular, so that the diagnosis may be very difficult. Signs of concomitant disease, such as adherent pericardium, valvular disease of the heart, pleural effusion, or renal disease, may be present. The urine is somewhat scanty and may present the characteristics of granular kidney. Jaundice is very rare, and when present is due to some complication.

Symptoms.—The onset is, as a rule, gradual; but symptoms may date from a febrile attack, and are usually vague. The first thing noticed is swelling of the abdomen followed by abdominal uneasiness and a sense of fulness and weight, but pain is absent or slight and only brought on by movement. There is naturally some loss of strength, and the muscles are flabby, but emaciation is slow in appearing. Patients may feel well and, except for the abdominal embarrassment, able to be up. Respiration may be somewhat hampered, constipation is usual and no doubt in part depends on the weakened state of the abdominal muscles, and there may be some flatulency and dyspepsia. Gastro-intestinal hemorrhage does not occur. In the later stages considerable wasting and œdema of the feet supervene. It is noteworthy that œdema of the feet occurs long after ascites has been well established.

The fluid varies to some extent in its characters. Usually it is like serum, of a citron color, and of a specific gravity of 1.015 or more. It may clot and form threads of fibrin or large flocculi. In some instances, in which subacute inflammation has supervened, it becomes turbid. It may be milky or chyliform, and after tapping blood-stained.

Diagnosis rests mainly on the presence of chronic and recurrent ascites, for which no other cause is forthcoming. It must be distinguished from other causes of ascites, such as tuberculous and malignant peritonitis and hepatic cirrhosis.

Prognosis.—This should be guarded; recovery is rare, but the course is slow, and as many as 100 tappings may be required. Some cases of the recurrent ascites which are diagnosed as simple chronic peritonitis certainly recover after a number of tappings. Nicholls found that the duration varied between two and sixteen years. The average

duration of Ramsbottom's 9 cases was six hundred and twenty-four days.[1] Death is generally due to intercurrent infection, such as pneumonia, but in cases associated with adherent pericardium and chronic mediastinitis it may be due to cardiac failure.

Treatment should, in the first instance, be directed to the cause, such as renal disease, heart affections, or syphilis; otherwise it is palliative and symptomatic. No permanent good can be anticipated from laparotomy and the attempt to produce artificial adhesions on the lines of the operation for the relief of the ascites of portal cirrhosis of the liver. Paracentesis should be performed when required; often this gradually becomes more frequent and may be necessary every week.

Diuretics, such as novasurol or caffeine, may be employed from time to time, and tonics may be necessary. Good hygienic conditions and fresh air are desirable. It is not necessary for the patient to remain in bed in the earlier stages. Some relief to the feeling of weight in the distended abdomen may be obtained from the use of a binder or belt.

TUBERCULOSIS OF THE PERITONEUM AND TUBERCULOUS PERITONITIS

The ordinary clinical heading of tuberculous peritonitis covers cases with somewhat different morbid lesions; thus, although tuberculous inflammation confined to the peritoneum is, strictly speaking, all that is implied, it is customary to include cases having in addition tuberculous ulcers of the intestine and tuberculosis of the intra-abdominal lymphatic glands, since these conditions are commonly combined and often cannot be separated during life.

The *incidence* of peritoneal infection in tuberculosis has been differently estimated. In 531 cases of pulmonary tuberculosis examined after death at the Brompton Hospital, there was tuberculous peritonitis in 22, or 4.1 per cent. (Fowler and Godlee[2]). In 197 cases of tuberculosis at the Boston City Hospital the peritoneum was infected in 14, or 7.1 per cent. (Bottomley[3]). In 1393 cases of tuberculosis at Breslau there was tuberculous peritonitis in 226, or 16.2 per cent. (Borschke[4]). In 300 cases of fatal tuberculosis of various parts of the body at St. George's Hospital the peritoneum was affected in 56, or 18.6 per cent.

Etiology.—Age.—The disease may occur at any period of life, but it is rare in babies and in old age. Osler recorded a patient aged eighty-two years, while among 163 cases tabulated by Morley Fletcher,[5] eight were under one year. It is most frequent between twenty and forty years of age. The belief that the disease is commoner in children is probably the result of confusion between chronic intestinal disturbance with a distended abdomen, formerly spoken of as "tabes mesenterica," and true peritoneal tuberculosis. In 306 cases of tuberculous peritonitis

[1] *Medical Chronicle*, Manchester, 1906, **45**, 7.
[2] *Diseases of the Lungs*, p. 358, London, 1898.
[3] *Medical and Surgical Reports*, Boston City Hospital, 1900, p. 118.
[4] *Virchow's Archiv*, 1892, **127**, 121.
[5] *Diseases of Children* (Garrod, Batten, Thursfield), p. 242, 1913, London.

under the age of fifteen, nearly half were between the ages of three and seven years (Faludi[1]).

Sex.—In children the sex incidence is equal. In adults there is a marked divergence between statistics from postmortem records and those of operation. Postmortem records show that it is more frequent in males; in König's 107 cases, 89 were males. In operation cases females are greatly in excess; this depends on the frequency with which tuberculosis of the Fallopian tubes serves as the starting-point for peritoneal infection. It is more frequent in negroes than in whites.

Disposing Factors.—Cirrhosis of the liver shows a decided tendency to be complicated by peritoneal tuberculosis; thus in 584 cases of hepatic cirrhosis, tuberculous peritonitis occurred in 53, or 9 per cent. No doubt alcoholism favors the incidence of tuberculosis generally, but the catarrh of the intestine and the portal obstruction probably play a part in localizing the infection. Injury has, in some cases, preceded the onset of symptoms. Pregnancy, according to H. Kelly,[2] has a definite causal relation to tuberculous peritonitis; in 28 per cent. of his cases the illness was dated from childbirth or a miscarriage.

Bacteriology.—The bovine form of the tubercle bacillus was found by the English Commission on Tuberculosis (1911) in 14 out of 29 cases, and by the German Commission in 63 per cent. of the cases of abdominal tuberculosis investigated. In 71 cases in New York 44, or 62 per cent., were bovine; there were 12 adults with bovine tuberculosis in 3, or 25 per cent.; and 41 of 59 children, 69 per cent. of whom were bovine (Hess[3]).

Tubercle bacilli are comparatively seldom found in the peritoneal effusion by ordinary microscopic examination. This scarcity of bacilli in the fluid, also seen in tuberculous pleural effusion, is thought to depend on adhesion of the bacilli to the serous membrane. Injection of the ascitic fluid into guinea-pigs proves that bacilli are present.

Paths of Infection.—In generalized tuberculosis the miliary tubercles seen on the peritoneum are due to hemic infection, the bacilli reaching the peritoneum by the bloodvessels, but in these cases the peritoneum merely shares in the universal outburst of tubercles and is seldom inflamed. Tuberculous infection usually reaches the peritoneum through the lymphatics. The bacilli may be conveyed from the intestine and vermiform appendix, the lymphatic glands, the pleuræ, the suprarenals, prostate, vesiculæ seminales, and the testes.

It is remarkable how often tuberculous ulceration of the intestine secondary to pulmonary tuberculosis is seen without diffuse tuberculous peritonitis. Thus, among 382 fatal cases of pulmonary tuberculosis at the Brompton Hospital, London, tuberculous ulcers were present in the intestine in 296, or 77.5 per cent., while tuberculous peritonitis occurred in 15 only, or 4 per cent. (Fowler and Godlee). Among 2421 collected cases of pulmonary tuberculosis 11 per cent. showed tuberculous peritonitis (Mayo). The occurrence of tuberculous peritonitis secondary to primary intestinal tuberculosis is variously estimated. German

[1] *Jahr. f. Kinderh.*, 1905, **62**, 304.
[2] *Operative Gynecology*, 1906, **2**, 237.
[3] *Am. Jour. Med. Sci.*, 1908, **136**, 183.

statistics are to the effect that primary intestinal tuberculosis even in children is very rare, and among Borschke's 226 cases of tuberculous peritonitis not one was secondary to primary intestinal tuberculosis. British statistics give a percentage of primary intestinal tuberculosis in children ranging up to 28.1 per cent. of the cases of tuberculosis (Shennan[1]) and averaging 19 per cent. as against 4 per cent. in Germany and 3 (Harbitz[2]) to 1.3 (Hess) per cent. in the United States. In women tuberculous disease of the Fallopian tubes is a prolific source of tuberculous peritonitis. Primary tuberculosis of the peritoneum, in which there is no tuberculous focus elsewhere in the body, and in which the path by which bacilli reach the peritoneum is not obvious, is rare. Borschke's series of 226 cases contained only 2.

Morbid Anatomy.—A few words may first be devoted to localized tuberculosis of the peritoneum. Local tuberculosis is always present in the subserous tissues of tuberculous intestinal ulcers, and occasionally gives rise to localized peritonitis, as shown by tags of adhesions. There may be localized tuberculosis in the neighborhood of the vermiform appendix or Fallopian tubes. In some instances a hernial sac when operated upon has been found to show localized tuberculosis.

In tuberculous peritonitis the morbid appearances vary considerably. Strictly speaking, these distinct types of tuberculous peritonitis from a pathological point of view do not exist, for they overlap and one described form may be only the later stage of another. Dupré and Ribierre[3] divide tuberculous peritonitis into (1) acute forms: (*a*) miliary, part of a generalized tuberculosis with abdominal pain, vomiting and tympanites; (*b*) miliary tuberculosis of the peritoneum and pleuræ (*c*) miliary tuberculosis around the cecum resembling appendicitis. (2) Chronic forms—namely, those usually recognized in this country: (*a*) ascitic, due to miliary tubercles on the peritoneum; (*b*) caseous, ulcerating, or suppurative; (*c*) fibrous; (*d*) localized.

The following method of dividing the anatomical lesions depends on the amount of adhesions present: (1) the ascitic; (2) the loculated, including (*a*) suppurative or ulcerous and (*b*) encysted ascites; and (3) obliterative, called chronic fibroid tuberculosis by Osler, fibrous or adhesive by others.

1. In the ascitic form there are few or no adhesions, and the exudation is free in the peritoneum. There is miliary tuberculosis which may be acute, subacute, or chronic. In the more acute forms inflammation of the peritoneum is engrafted on to miliary tuberculosis. The small tubercles vary in size from that of a millet seed downward, are scattered over both layers of the peritoneum, mesenteries, and omentum, and are often more numerous over the diaphragm. In the chronic forms the tubercles are larger, fibrotic, and are often somewhat pigmented; the peritoneum is thickened and the naked-eye appearances may exactly imitate those of malignant disease. The omentum becomes rolled up into a hard mass, the mesentery is shortened from cicatricial contraction

[1] *Edinburgh Hos. Rep.*, 1900, **6**, 130.
[2] *Jour, Infec, Dis.*, 1905, **2**, 189.
[3] *Nouveau traité de médicine* (Brouardel, Gilbert, Thoinet), 1909, **18**, 175.

so that the intestines become tethered to the spinal column, and from a similar process the intestine becomes shortened in length. These changes resemble those in simple chronic peritonitis.

Pseudotuberculosis is very rare. Dévé[1] described multiple granulomas on the peritoneum enclosing fragments of hydatid membrane and hooklets in cases of rupture of a hydatid cyst; a similar appearance may be due to multiple minute cysts. Pseudotuberculosis due to the ova of parasites, and to cholesterol plates has been recorded (Hebling; Miura).

2. The loculated or encysted form of peritonitis may be (*a*) suppurative or ulcerated or (*b*) ascitic. (*a*) In the most characteristic and serious form the intestines are matted together by adhesions and enclose collections of serofibrinous, turbid, or purulent exudation. In this form the tubercles increase in size, become confluent masses of caseous material surrounded by fibrin and adhesions, and by softening give rise to suppurating foci among the adherent coils of intestine. There may thus be numbers of intraperitoneal abscesses, the pus of which may erode the walls of the intestine and eventually lead to perforation, and as a result a fecal fistula may form at the umbilicus. Purulent foci may also open into the vagina; in such cases the tubes were probably the original focus of infection. On attempting to unravel the intestines in such a case the bowel is easily torn, and it is sometimes difficult to be certain whether perforation was present during life or was made at the necropsy. The adhesions unite all the viscera; the omentum is thickened, contains caseous tubercles, and is usually rolled up into a firm cord. The mesenteric glands are enlarged and caseous; they may soften and give rise to a circumscribed abscess, which in a case seen by the writer imitated a pancreatic cyst.

(*b*) In the ascitic form of loculated tuberculous peritonitis there is a transition between the ascitic and obliterative forms.

3. The obliterative (chronic fibroid or adhesive) form may follow cure of the ascitic form or develop subacutely. The inflammatory process leads to universal adhesions which unite all the abdominal viscera inextricably to each other and to the abdominal wall; as a result there is no exudation. The tubercles tend to undergo fibrotic changes and show pigmentation. The matted intestines, the rolled up omentum, and masses of caseous glands embedded in adhesions give rise to the tumor-like masses felt through the abdominal wall. In exceptional instances large pendulous caseous masses, resembling "Perlsucht" in animals, have been described in man (MacCallum[2]).

Tuberculous peritonitis may be associated with cirrhosis of the liver, and in the vast majority of cases the hepatic change is the older. In some cases the serous membranes—pleuræ and peritoneum—seem especially liable to tuberculous infection, and may be notably affected, although there is little evidence of tuberculosis elsewhere in the body. The lymphatic glands in the anterior mediastinum are infiltrated with tubercles as the result of infection from the abdomen.

[1] *Arch. de méd. exper. et. d'anat. path.*, Paris, 1907, **19**, 347.
[2] *Johns Hopkins Hospital Bull.*, 1901, **12**, 293.

Symptoms.—These vary quite considerably according to the anatomical lesions present. In generalized miliary tuberculosis the infection of the peritoneum may be latent, and, there being no effusion, the peritoneal infection is not suspected during life unless there be abdominal pain or retention of urine and difficulty and pain in micturition. In local peritoneal tuberculosis there may be local pain and tenderness; this may be seen in the neighborhood of the vermiform appendix, and then suggests appendicitis.

The anatomical forms into which diffuse tuberculous peritonitis has been divided may to some extent be correlated with corresponding groups of symptoms and physical signs.

1. In the *ascitic* form, in which miliary tubercles are scattered over the peritoneum, the characteristic feature is the effusion. The onset is usually gradual and preceded by failing health, loss of appetite, strength, and weight, with some abdominal discomfort or pain. The abdomen becomes swollen and tumid, often mainly tympanitic at first, and in children the condition may resemble that of chronic intestinal catarrh. As the case progresses the distention is gradually seen to be not entirely tympanitic, and evidence of free fluid becomes obvious and more distinct. In some cases the onset of ascites is sudden. As a rule, the amount of fluid is not extreme, and if removed reaccumulates slowly; but in adults with existing hepatic cirrhosis the ascitic distention may be indistinguishable from that due to uncomplicated cirrhosis. The distended abdomen is tender on pressure. The pressure of a large ascitic effusion on the inferior vena cava may cause some œdema of the feet and even a trace of albumin in the urine. The ascitic fluid may be clear, turbid, or even blood-stained, and may coagulate when removed. As pointed out elsewhere, the contained cells are mainly lymphocytes. The opsonic index of the effusion is lower than that of the blood serum.

2. (*a*) The *suppurative* or *ulcerative* form of encysted tuberculous peritonitis is the most characteristic. The onset of abdominal symptoms is, as in the ascitic form, preceded by failing health and an irregular temperature. The abdomen becomes swollen and tumid, often first in the lower part, and there is a complaint of abdominal discomfort and tenderness, and of griping pains. The abdominal pain is made worse by walking and by jarring. The abdomen gradually becomes more distended, and the existence of fluid is suspected, but being more or less encysted is often difficult to determine. On palpation the abdomen feels doughy and tumor-like masses due to enlarged glands, adherent coils of intestine, or the rolled up omentum may be felt through the abdominal wall. The thickened omentum forms a characteristic hard cord running transversely across the upper part of the abdomen; there is usually resonance above it, which enables it to be distinguished from the margin of the liver. The tumors are usually fixed, tender on pressure and usually dull on percussion. The amount of distention and the distinctness with which these pseudotumors can be felt vary from time to time. This depends on changes in the amount of exudation and in the quantity of gas in the intestines. In advanced cases the umbilicus may become indurated and inflamed from an abscess pointing there;

although this should always suggest the possibility of tuberculous peritonitis, it is not pathognomonic, for a localized pneumococcic abscess may discharge at the umbilicus, and so may an abscess in puerperal infection. Percussion is painful and shows irregular areas of resonance, due to tympanitic distention of intestinal coils, and of dulness due to localized exudation. Rectal or vaginal examination may reveal the presence of tumors due to glands, matted coils of intestine, or salpingitis.

(*b*) In the ascitic form of encysted peritonitis the collection of serous fluid may simulate an abdominal cyst, especially in women.

3. In the *obliterative* form the clinical manifestations are often vague. They may be mainly those due to interference with the functional activity of the alimentary canal, dyspepsia, flatulence, constipation, and pain; or there may be palpable tumors. Some cases with universal adhesions may not present any symptoms, but in others the intestinal movements may be so interfered with as to give rise to chronic obstruction. Symptoms of chronic intestinal obstruction may be brought about by peritoneal adhesions at one point; or in rare instances numerous peritoneal adhesions, no one of which produces definite obstruction, may so obstruct the intestines as to give rise to chronic obstruction; in such a case in a child the visible contracting coils of intestine may be seen through the abdominal wall.

The spleen and less often the liver may be enlarged. Very considerable hepatic enlargement may be due to fatty change, or to concomitant backward pressure. In boys with a patent funicular process between the peritoneal cavity and the tunica vaginalis testis tuberculous thickening may spread down the cord, and hydrocele may result.

The abdominal walls may show prominent subcutaneous veins, and the skin may become harsh, dry, and lose its elasticity. But with abdominal distention it may become shiny; in some instances it is pigmented, and sometimes pigmentation is also seen on the face and may be regarded as indicating some degree of suprarenal insufficiency. There is often a drawn expression, and the face shows signs of grave illness. The condition of the tongue varies; it may be red, irritable, and denuded of epithelium, or furred. Nausea, vomiting, and hiccough are rare. The stools may be colorless and fatty, especially in children, but this change occurs in other cachectic conditions. The temperature is raised in acute and suppurative cases, and may touch 104° F. In many cases there is but slight fever, and in the chronic forms there may be none. From abdominal distention and upward displacement of the diaphragm respiration is embarrassed, and the respiratory movements are rapid, shallow, and mainly costal. The pulse becomes rapid in acute cases, but in the chronic forms is not affected.

The urine does not contain the large quantities of indican seen in acute peritonitis. Albuminuria is not generally considered to be frequent, but Hamman found it in 81 out of 133 cases. Micturition may be painful. In females tubercle bacilli may be found in the vaginal discharge.

The blood shows a moderate secondary anemia, but from concentration of the blood due to ascites or purging there may be an apparent polycythemia. Leukocytosis occurs in a certain number of the cases (40

per cent., Emerson; 30 per cent., Shattuck; and 23 per cent., Cabot), but is due to some complication or secondary infection. A high leukocyte count is more often seen in children.

Jaundice from compression of the ducts by adhesions has been recorded (Dujon[1]), and may also be due to the pressure exerted by tuberculous glands in the portal fissure, but even this is rare. Ulceration of a tuberculous gland into the hepatic artery has been known to produce an aneurism (Birkhardt and Schümann[2]).

Complications.—Extensive tuberculous ulceration of the intestine, especially of the colon, may be suspected when there is diarrhœa with offensive stools and blood; examination may show tubercle bacilli in the feces. Acute or subacute symptoms suggesting appendicitis, cholecystitis, or pelvic peritonitis may be due to an eruption of miliary tubercles over the peritoneum without any ascites (Armand-Delille[3]). Acute peritonitis may supervene as the result of rupture of a suppurating gland or from perforation of a tuberculous intestinal ulcer. Intestinal obstruction is not so common as might be anticipated; Aimes[4] who collected 64 cases found that the commonest cause was a band, other factors were matting of the intestines and intestinal paralysis which may be due to thrombosis. In all three forms the obstruction is far more often acute than chronic.

The thoracic complications are pulmonary tuberculosis and pleurisy, which may be bilateral. A tuberculous pleurisy may exist at the same time as an active tuberculous peritonitis, precede it, or come on when the peritoneal lesion has ceased to be clinically manifest. Symptoms suggesting subacute intestinal obstruction—namely, constipation and vomiting—may be in reality due to the onset of tuberculous meningitis.

Diagnosis.—The presence of tuberculosis elsewhere is an important factor. In children tuberculous infection of the peritoneum is much the commonest cause of ascites. In women the association of disease of the uterine adnexa should always suggest a tuberculous origin for ascites or chronic peritonitis.

In some rather rare cases there may for a time be a very considerable resemblance to typhoid fever. The most certain means of distinguishing between these two conditions is by a blood-culture or by the agglutination reaction. When tuberculous peritonitis comes on acutely there may be very great difficulty in deciding whether the condition is due to pneumococcic or tuberculous infection.

It may be very difficult to avoid mistakes in the diagnosis between the ascites of tuberculous peritonitis and that of hepatic cirrhosis. In children hepatic cirrhosis is rare, and when it gives rise to ascites tuberculous peritonitis is very likely to be diagnosed. In adults the diagnosis is not so difficult, as help is obtained from a history pointing to alcoholism or from the presence of tuberculosis elsewhere. But alcoholism disposes both to cirrhosis and to tuberculosis, and pulmonary tuberculosis

[1] *Procès-verbaux, XIX Congrès de chir.*, 1906, 166.
[2] *Deutsch. Arch. f. klin. Med.*, 1907, **90**, 288
[3] *Presse méd.*, Paris, 1912, **21**, 397.
[4] *Rev. de chir.*, Paris, 1920, **58**, 177.

is not uncommon in cirrhosis. Further, tuberculous peritonitis may supervene in the course of hepatic cirrhosis, and when this occurs the true nature of the ascites is not likely to be suspected until the fluid is examined. (For cytological diagnosis see pages 820 and 904.)

Simple chronic peritonitis is afebrile, there is less pain, and examination of the fluid after tapping should assist in making a diagnosis. Some assistance may be obtained by estimation of the opsonic index before and after abdominal massage, a considerable rise in the index pointing to tuberculosis.

Difficulty sometimes arises in deciding whether abdominal distention with fluid and the presence of tumors—omental and glandular—are due to tuberculosis or to malignant disease. In some cases a diagnosis is only made by opening the abdomen. As a rule, irregular fever and a history pointing to tuberculosis favor tuberculous infection, which in children is much commoner than is intra-abdominal sarcoma. An appeal to the therapeutic test of heliotherapy has been advocated (Boles[1]). In adults the presence of multiple tumors is more probably evidence of malignant disease. Cases of chronic intussusception in children have been regarded as tuberculous peritonitis.

Prognosis.—This may be considered from several points of view: (*a*) as to immediate recovery; (*b*) as to relapses of the peritoneal infection; (*c*) as to complications and remote mechanical effects of adhesions.

(*a*) As to immediate recovery. The prognosis is different in the various forms of peritoneal tuberculosis. The disease may become arrested and the symptoms disappear without any manifest cause. The improvement may be permanent or only temporary. The prognosis is best in the discrete miliary form with ascites when uncomplicated, and worse in the form with numerous localized foci of purulent exudation. According to F. Taylor, tuberculous peritonitis is probably fatal in more than half the cases, but the general impression is that the outlook is more hopeful than this and that cure occurs in 50 per cent. In estimating the outlook in an individual case, the condition of the general nutrition, the evidence of tuberculosis elsewhere, as in the lungs, the presence of diarrhœa and of fever must be taken into account. The more acute the onset, the worse the prognosis. An increased excretion of chlorides in the urine is said to be a sign of improvement. Wasting diarrhœa and persistent fever are bad signs. The prognosis is bad in the presence of complications such as extensive ulceration of the intestines, well-established pulmonary tuberculosis, generalized tuberculosis, meningitis, and evidence suggesting rupture of a suppurating mesenteric gland into the peritoneal cavity. According to H. T. Ashby[2] the prognosis is practically hopeless in the first year of life, and but little better in the second year. The presence of pleurisy does not make the prognosis worse. An abdominal abscess is a grave sign, but recovery may follow discharge of pus from the umbilicus; a fecal fistula is nearly always fatal.

(*b*) Recurrence occurs in a certain number of cases. This probably depends on the presence of some source of reinfection in the abdominal

[1] *Jour. Am. Med. Assn.*, 1924, **82**, 2112.
[2] *Brit. Med. Jour.*, 1923, ii, 863.

cavity—namely, in the intestine, lymphatic glands, vermiform appendix or the Fallopian tubes. The importance of removing the local focus whenever possible has been shown by W. Mayo.[1] On the other hand, in 122 cases of tuberculous peritonitis at all ages, Stone[2] did not find a primary focus in the Fallopian tubes or the vermiform appendix in any case. But the Fallopian tubes are often infected from the peritoneum.

(*c*) Generalized tuberculosis occurs in a considerable proportion of the fatal cases in children; in 26 fatal cases this was noted in 13 (Rolleston[3]). The remote mechanical effects are due to peritoneal adhesions which may give rise to internal strangulation of the intestine and acute obstruction. Undoubtedly a considerable proportion of the cases of strangulation by bands occur in patients who have suffered from tuberculous peritonitis, but the number of cases of tuberculous peritonitis in which acute obstruction is due to a band must be small. Since tubercles and peritoneal adhesions may completely disappear, the persistence of adhesions probably depends on a particularly severe form of peritonitis or, more probably, on the persistence of a tuberculous focus in the peritoneal cavity.

Treatment may be divided into (1) medical, (2) by injection of vaccines, (3) hygienic measures, (4) heliotherapy and roentgen-ray treatment and (5) by surgical means.

Medical.—The patient should be kept in bed in a well-lighted and airy room. The bowels should be regulated, any tendency to diarrhœa controlled, and constipation obviated. Offensive stools should be treated by guaiacol, which is less irritating than creosote, or if offensive and loose, by salicylate of bismuth. Cod-liver oil and the syrup of the iodide of iron may be given with advantage, but the dose of cod-liver oil should be small at first and the stools should be examined to see that it is being assimilated. Mercurial or iodoform ointment, or guaiacol (℥j) in anhydrous lanolin (℥j) may be rubbed into the skin of the abdomen, which is then covered by a flannel binder. Good results, however, have been reported simply from bandaging.

Vaccine.—Treatment is stated to be sometimes successful. Tuberculin (Koch's new tuberculin; T.R.) in doses of $\frac{1}{20000}$ mg. of the powdered vaccine is given hypodermically, and is not increased above $\frac{1}{6000}$ mg. Riviere[4] advises $\frac{1}{12000}$ to $\frac{1}{8000}$ mg. for a child of one year, $\frac{1}{4000}$ mg. for a child of five years, and $\frac{1}{3000}$ mg. for children of ten to twelve years. If human tuberculin fails a trial may be given to bovine tuberculin.

Heliotherapy.—Heliotherapy as advocated by Rollier,[5] who strenuously opposes operative interference, has had remarkable success; but it requires due caution, especially in the caseous form, and the exposures should begin on the feet and gradually be carried upward. Cases with concomitant tuberculous pleurisy also react extremely well.

Roentgen-ray exposures of the abdomen at intervals of three weeks, a

1 *Jour. Am. Med. Assn.*, 1904, **44**, 1157.
2 *Boston Med. and Surg. Jour.*, 1908, **158**, 705.
3 *Brit. Med. Jour.*, 1911, ii, 473.
4 *Brit. Med. Jour.*, 1907, ii, 1131; and *Tuberculin Treatment*, 1913, Oxford.
5 *Heliotherapy*, 1923, p. 96. Oxford Medical Publication and *Die Heliotherapie der Tuberculose*, Berlin, 1924, **5**, 102.

different area being irradiated each week, have given brilliant results in a large number of cases under Bircher.[1] Ultraviolet rays are also said to have been followed by good results (Pletney;[2] Gerstenberg and Wahl[3]).

Hygienic Treatment.—Very satisfactory results follow moving the patient in the early stages into the country and especially to the seaside, with the adoption of open-air treatment. This should be adopted as early as possible, and continued until recovery has been established.

Surgical Treatment.—Laparotomy is contra-indicated in widespread tuberculosis, in infants under a year old and in the presence of pulmonary tuberculosis. It is necessary when an abscess forms or when acute intestinal obstruction occurs; and it is useless in the obliterative and adhesive form. In 1890 König published 131 cases, with 84 recoveries. It was supposed that operation reduced the rather feeble vitality of the peritoneal tubercles, and thus led to their death. The way in which the withdrawal of fluid acts may be explained in the following manner: peritoneal tuberculosis, being a local infection, the opsonic index of the ascitic fluid is lower than that of the blood-plasma; hence, if the ascitic fluid be removed, it enables a fresh effusion from the blood to occur; the opsonic index of this recurrent effusion is higher than that of the original one, and therefore exerts a curative effect. If this were the only object, simple paracentesis should be equally effective. Cures have followed paracentesis alone, or followed by the injection of an emulsion of iodoform, of air or of oxygen into the peritoneum. The utility of laparotomy is, however, by no means confined to removal of the ascites; it is important to take away, when possible, the primary focus of tuberculous infection, such as the Fallopian tubes or the vermiform appendix, so as to prevent continued infection and a relapse. Apart from this consideration it is most successful in ascitic cases which are those that respond best to other methods. The question whether laparotomy gives better results than medical treatment has been extensively discussed, and numerous statistics have been brought forward to support the respective lines of treatment. Rendle Short[4] concludes that non-surgical treatment cures about one-third of the cases, and that of those operated upon about one-half remain permanently well.

Other forms of treatment should be tried first, and if improvement follows should be persisted in. If improvement does not occur in four or six weeks operation is indicated, unless there be some reason to the contrary. Any sign of increase in the activity of the disease should lead to earlier operation.

TUMORS OF THE PERITONEUM

The subject of new-growths of the peritoneum will be considered under the following heads:

1. Non-malignant tumors. (*a*) Solid. (*b*) Cystic.
2. Malignant growths. (*a*) Primary. (*b*) Secondary.

[1] *Strahlentherap.*, 1920, **2**, 646.
[2] *Arch. Clin. und exper. Med.*, Moscow, 1922, **50**, 24.
[3] *Jour. Am. Med. Assn.*, 1924, **83**, 1631.
[4] *An Index of Prognosis*, Bristol, 1922, p. 426.

Non-malignant Tumors

These are not so rare as primary malignant tumors of the peritoneum, but this is mainly due to the inclusion, among innocent tumors, of cysts which are commoner than the solid innocent growths.

Solid Non-malignant Tumors.—Fibromas, Fibromyomas, and Myomas.—In the first place circumscribed thickenings of the peritoneum due to attrition, such as the lamellar fibromas on the surface of an enlarged spleen, or those due to chronic inflammation, such as the fibrous plaques sometimes present in chronic peritonitis, fibrosed tubercles, and pseudo-tubercles must be excluded from consideration. A lamellar fibroma has been known to form around a piece of steel (Shattock[1]).

Although not intraperitoneal tumors, attention may be directed to the fibrous desmoid tumors of the anterior abdominal wall, which, although innocent, are sometimes erroneously described as fibrosarcomas. They occur mainly in women, especially in multiparæ and during pregnancy, and it has been said that the protuberance of the abdomen favors their development. They are more often below than above the umbilicus; they are equally common on the right and left sides. They arise from the sheath of the rectus muscle, from the neighboring aponeuroses, from the iliac crest (Nélaton), from tendons (Doran), or possibly from the round ligament of the uterus. They may be multiple. In 400 cases of connective-tissue tumors of the abdominal wall collected by Pfeiffer,[2] 87 per cent. were in women.

Pure *fibromas* are rare, they are usually single and of considerable size, and are found in connection with the mesentery, omentum, or the retroperitoneal space. They probably arise from proliferation of pre-existing fibrous tissue in these positions, but Belkowsky[3] described a hard fibroma which he believed was derived from an appendix epiploica. Whitney[4] described a special group of fibromas arising from the sub-peritoneal tissues of the true pelvis. The tumors are composed of œdematous fibrous tissue enclosing some endothelial cells, and may produce hernial protrusions in the perineum, ischiorectal region, labium, or scrotum. Of Whitney's 19 cases, 15 were females and 4 males. They may reach a very considerable size.

Some apparently fibrous tumors growing from the retroperitoneal space and from the root of the mesentery contain smooth muscular fibres, which may be derived from Treitz's muscle in the root of the mesentery, and are really fibromyomas. The tumor may pass between the layers of the mesentery and form a solid mesenteric tumor. Solid non-malignant tumors of the mesentery, of which the number was brought up to 39 by MacAuley[5] in 1925, have been thought to arise from the connective tissue of the mesentery, from the wall of the intestine, or to be detached uterine fibromyoma. In 32 cases of fibroma, fibromyomas, or myoma of the mesentery, collected by Greer,[6] 11 were in females, thus disproving

1 *Transactions of the Pathological Society of London*, 1893, **44**, 151.
2 *Beitr. z. klin. Chir.*, Tübingen, 1904, **44**, 334.
3 *Rev. méd. de la Suisse Romande*, Geneva, 1893, 431.
4 *Ann. Surgery*, 1905, **41**, 823.
5 *Irish Jour. Med. Sci.*, 1923, 5th ser., 54.
6 *Brit. Med. Jour.*, 1911, ii, 1085.

the view that these tumors are necessarily of uterine or broad ligament origin. Fibromas and fibromyomas are encapsulated and shell out readily; they may show mucoid degeneration with the formation of spaces in their substance, and so resemble cystic fibromyomas of the uterus. Fibromyomas, or possibly in rare instances myomas, of retroperitoneal origin may be multiple.

Ganglionated neuromas of the mesentery have been recorded (Macnoughton-Jones;[1] P. Paterson;[2] Bland-Sutton[3]) they may eventually become malignant neuroblastomas.

The *clinical aspects* depend upon the position of the tumor. The special feature of the fibromas arising in the true pelvis—viz., the tendency to give rise to hernial protrusions—has already been referred to. The symptoms come on slowly, pain is absent in most instances, and intestinal obstruction, which is not uncommonly brought about by mesenteric cysts, does not seem to occur. The correct diagnosis is very difficult, and these tumors are very likely to be regarded as ovarian cysts or uterine fibromyomas.

The *treatment* is surgical, and consists in removal. Of 27 fibromas or fibromyomas of the mesentery removed by operation, 20 recovered (Greer). A *ganglionated neuroma* derived from the sympathetic has been found in the mesentery (McNaughton Jones[4]) and a neuromyoma of the mesentery has been described (Paterson[5]).

Lipomas may arise in the abdominal cavity (1) in connection with hernial orifices, the inguinal, femoral, or obturator rings, and in weak spots or defects in the linea alba. Overgrowth of fat in these positions may exert traction and so pull out a process of the parietal peritoneum and thus give rise to hernia. They may cause pain and vomiting, which, unless their presence is detected, are difficult to explain. (2) In rare instances they arise from giant-growth of an appendix epiploica; Gruber[6] recorded a large pedunculated lipoma which formed the only content of a left scrotal hernia. (3) From the fat around the kidneys, in the iliac fossæ, or pelvis; they lie under the prerenal fascia which separates them from the colon, intestines, and pancreas. These lipomas are rather more common on the right side and may remain retroperitoneal, or may work their way between the layers of the mesentery, mesocolon, omentum, or, in rare instances, of the broad ligament and so become more or less pedunculated. On the basis of an analysis of 152 collected cases Wahlendorf[7] estimated that 79 per cent. are abdominal and 21 per cent. pelvic. The transverse colon may become surrounded by the adipose growth. They are usually single, but may show signs of fusion of separate tumors. They may be composed of fat only or of fat mixed with fibrous tissue, show myxomatous degeneration, calcareous infiltration, or very rarely contain cartilage. Very exceptionally sarcomatous change has supervened. They may be encapsuled, or shade off into the retroperitoneal fat from which they arise. Most of the recorded instances have

[1] *Proc. Roy. Soc. Med.*, 1912, **5** (Obst. and Gyn. Sect.), 287.
[2] *Lancet*, 1913, ii, 997.
[3] *Ibid.*, 1918, i, 429.
[4] *Proc. Roy. Soc. Med.*, 1912, **5**, (Sect. Obst.), 237.
[5] *Lancet*, London, 1913, ii, 997.
[6] *Virchow's Archiv*, 1885, **102**, 541.
[7] *Arch. f. klin. Chir.*, 1921, **115**, 751.

weighed over 20 pounds, and about 6 have been more than 50 pounds. In Buckner's[1] case, a fibrolipoma arising in the subperitoneal tissue of the true pelvis weighed 268 pounds.

Etiology.—The large lipomas, which are decidedly rare, are more frequent in women than in men, 72 females to 28 men (Wahlendorf). The usual age is between thirty and fifty years, but isolated examples have been recorded in children. They are not necessarily associated with general obesity. Of Proust and Treves' 89 collected cases, 14 were parietal, 38 perirenal, and 37 mesenteric. Ten were multiple and the remainder single tumors.

Physical Signs.—Unless of a large size, they are not likely to be detected, as from their soft consistency they are difficult to feel. They grow slowly, so that the increase in size of the abdomen is gradual. When palpable, the tumor is soft, smooth, free from tenderness, and semifluctuating, so that ascites, either general or encysted, is commonly suspected, although ovarian or hydatid cysts have been diagnosed. As growth proceeds, the abdominal distention, which is mainly in the anteroposterior diameter, increases, the diaphragm is pushed up and the contents of the thorax pressed upon. The later stages are attended with general wasting and œdema of the feet; malignant disease may then appear probable.

Symptoms.—The progress of the disease is slow, the general health and nutrition are well maintained, and symptoms do not appear for a long time. They include a feeling of weight, fulness, and discomfort from abdominal distention, sometimes gastro-intestinal symptoms from pressure on the stomach and intestines, inconvenience from pressure on the urinary bladder, and sooner or later dyspnœa from the upward displacement of the diaphragm.

Diagnosis from ascites is extremely difficult, as such a rare condition as a lipoma is only likely to be suspected after the abdomen has been unsuccessfully tapped. From malignant disease their slow course is the main distinction. From ovarian and hydatid cysts they differ in their softness and indefinite outlines. Difficulty has occurred in distinguishing them from large lipomas of the abdominal wall.

Prognosis.—This depends upon their being operated upon before they have reached a very large size, for if left alone the patients gradually emaciate and die. In 26 cases in which the tumor was wholly or partially removed, recovery followed in 12, with recurrence in one (Adami[2]).

Treatment.—The only radical method is surgical, but the results of removal differ in those that are entirely retroperitoneal and in those that are pedunculated or situated in the omentum. Removal of a retroperitoneal lipoma has, in some cases, deprived a considerable extent of the intestine of its blood-supply, and so led to gangrene or necessitated resection of part of the intestine. The operative mortality varies from 16 to 25 per cent. (Greensfelder and Bettmann[3]).

[1] Quoted by Whitney: *Ann. Surg.*, 1905, **41**, 823.
[2] *Montreal Med. Jour.*, 1897, **25**, 620.
[3] *Surg., Gynec., and Obst.*, 1923, **37**, 468.

Angioma is very rare, but the line dividing them from angiosarcoma is rather thin. In Julliard's[1] case a cavernous angioma of the mesentery was as large as an adult's head, and produced intestinal obstruction. Lane[2] successfully removed a large degenerating cavernous angioma from the peritoneum of a child aged seven years. A cystic lymphangioma forming a subperitoneal tumor in the pelvis of a boy aged seven years described by Landelius[3] appears to be closely allied to other retroperitoneal cysts.

Myxoma.—Myxomatous degeneration, of course, occurs in fibromas, myomas, and lipomas, and in some instances the condition may be so advanced as to appear to be a pure myxoma.

Cysts.—*Parasitic.* Hydatids, cysticercus.

Non-parasitic.—Mesenteric, omental, sanguineous, retroperitoneal hematoma, dermoid, retroperitoneal, urachal, conditions simulating cysts.

Hydatid Disease of the Peritoneum.—Infection of the peritoneum with the cystic or bladder stage of the *Tænia echinococcus*, although very striking, is not common; thus, in 1897 cases of hydatid disease, tabulated by Davies Thomas,[4] the peritoneum, omentum, and mesentery were affected primarily in 26, or 1.4 per cent., only. From a review of 2727 cases Dévé[5] concludes that peritoneal hydatidosis is always secondary. No statistics exist to show that hydatid disease of the peritoneum was commoner in the early part of the last century when Bright gave such a graphic account of its clinical features, but the practice then in vogue of tapping these cysts through the abdominal walls with a trocar offered great facilities for infection of the peritoneal cavity.

The method by which infection of the peritoneum with hydatid cysts takes place is probably not always the same. In cases with a large number of cysts implanted on the peritoneum the most probable explanation is that rupture or leakage from a single and primary cyst, usually in the liver, has infected the peritoneum. It appears to take about two years for cysts thus implanted on the peritoneum to become sufficiently large to give rise to signs and symptoms. Admixture of bile with ascitic fluid does not prevent secondary infection of the peritoneum with hydatid cysts. On the other hand, in instances in which a single cyst or only a few cysts occur in the retroperitoneal tissue, a very common position being between the prostate and the rectovesical fascia, the embryo may have burrowed from the bowel or from the bloodvessels in the neighborhood toward the peritoneum. Cranwell,[6] who has collected 56 examples of retrovesical hydatid cysts in males, believes that most of the retrovesical cysts are due to peritoneal infection.

Morbid Anatomy.—The number of cysts may be enormous when the infection is secondary to rupture of a preëxisting cyst; the omentum, mesentery, and visceral peritoneum may be almost universally affected,

[1] *Rev. de gyn. et de chir. abdom.*, 1904, **8**, 229.
[2] *Trans. Clin. Soc.*, London, 1893, **26**, 5.
[3] *Acta chir. Scandinav.*, Stockholm, 1923, **56**, 76.
[4] *Hydatid Disease*, Adelaide, 1884.
[5] *Compt. rend. Soc. biol.*, Paris, 1913, **74**, 735.
[6] *Rev. de gyn. et de chir. abdom.*, Paris, 1907, **11**, 606.

but the omentum and pelvis are the most frequent sites. The cysts may be of almost any size, from a pinhead upward; when single or few, the cysts tend to be bigger than when large numbers are present. The cysts may project from the surface of the viscera, be sessile on the peritoneum, especially on the omentum, mesentery, and pelvis, be pedunculated, and in rare instances a cyst may lie free in the abdominal cavity. Pedunculated hydatids may be sterile, probably from a deficient nourishment. The cysts may be separate or crowded together. According to Stirling and Verco,[1] adhesions around uninflamed cysts occur only after injury or operative interference. Chronic peritonitis may be set up by mechanical irritation, and may lead to the formation of a thick fibrous capsule over dependent or other cysts, such as those in Douglas' pouch, exposed to friction; calcification may subsequently occur. A rare condition of "pseudotuberculosis" of the peritoneum may follow rupture of a cyst, and consists of (1) minute developing cysts and (2) of small nodular granulomas containing hooklets or pieces of hydatid membrane scattered over the surface of the peritoneum.

Suppuration may take place in one or more of the cysts and set up a localized abscess, general peritonitis, or pylephlebitis and multiple abscesses in the liver.

Clinical Aspect.—The enlargement of the abdomen is gradual, and may continue for years; in one of Bright's[2] cases it had lasted for at least ten years. There may be either a diffuse swelling, or separate cysts can be made out, not only by palpation, but with the eye. The cystic tumors are often so firm as to suggest solid growths, they are freely movable, alter their position with that of the body, and are not obviously connected with any of the abdominal viscera. A hydatid thrill is rare, and as it may be present over other cysts, such as ovarian or mesenteric, and even in ascites, too much stress must not be laid on it. When the abdomen becomes very greatly distended the diaphragm is pressed up and respiration is much embarrassed, while pressure on the stomach and intestines may lead to dyspepsia, constipation, or, in very rare instances, to intestinal obstruction. As the result of pressure on the inferior vena cava, the superficial abdominal veins may become very prominent and the urine scanty and high-colored. In rare instances ascites, either of mechanical or inflammatory origin, may occur in cases of intrahepatic hydatid (Robin, Weil, and Bith[3]). A retrovesical cyst in the pelvis may press on the rectum, bladder, and ureters, and imitate a hypertrophied prostate, or lead to hydronephrosis, consecutive kidney disease, and pyelonephritis. Out of 24 autopsies on such cases, the ureters were dilated in 11 (Cranwell). There is vesical pain, frequent micturition, constipation, and a feeling of weight in the perineum.

Diagnosis.—If multiple cystic tumors can be felt, the true solution is not difficult, but when the patient is a woman and one or two cysts only are palpable, the disease may be thought to be ovarian cystadenomas or even uterine fibromyomas. The history that a hydatid cyst of the

[1] *System of Medicine* (Allbutt and Rolleston), vol. **2**, Part 2, p. 999.
[2] *Clinical Memoirs on Abdominal Tumors.* New Sydenham Society, 1860.
[3] *Ann. de méd.*, Paris, 1920, **7**, 85.

liver has existed or has been tapped would be strongly in favor of hydatid infection of the peritoneum. From multiple abdominal malignant disease the slow course and evidence that the tumors are cystic should distinguish it. Exploratory puncture is dangerous, as anaphylactic symptoms and even death may follow escape of hydatid fluid into the peritoneal cavity. If it be done, the discovery of scolices, hooklets, or of the characteristic laminated ectocyst, proves that a hydatid had been aspirated; chemical analysis, however, does not settle the question, for some hydronephroses contain fluid of a very similar composition. Eosinophilia, a specific precipitin reaction, and fixation of the complement when positive point to hydatid infection, but a negative result is inconclusive. A stable preparation of hydatid for the complement-fixation test has been obtained by Patterson and Williams.[1]

Treatment.—A single cyst should be fully exposed and dealt with surgically; when the cysts are manifestly multiple, operation is not likely to be so satisfactory as with a single cyst. Dévé[2] urges that large sessile cysts should be injected with formol (2 per cent.) and the contents removed, and that small sessile cysts should be injected with formol only. In no case should a cyst be tapped through the abdominal wall. A single cyst in the pelvis may be opened through the perineum or vagina. The outlook in these retrovesical cysts is grave, as of 56 cases 25 proved fatal (Cranwell). Arcé's[3] observations suggest that deep roentgen-ray therapy kills the parasite and so enables small cysts to become obsolescent.

Cysticercus cellulosæ is, in rare instances, met with in great numbers inside the abdomen, chiefly in the mesentery, but this condition gives rise either to insignificant or to no clinical symptoms.

Mesenteric Cysts.—This term has sometimes been applied to cysts in the omentum and mesocolon, but it is better to limit it to cysts in the mesentery of the small intestine and to employ it solely as descriptive of the position of the cyst. According to Higgins and Lloyd[4] 250 cases have been reported since Benevieni, the Florentine anatomist, described the condition in the Sixteenth Century.

Pathogeny.—Proust and Monod[5] describe the following forms of mesenteric cyst: (1) Derived from the remains of embryonic epithelium (*a*) of intestinal origin; Terrier and Lecène[6] collected 18 "enteroid" or juxta-intestinal cysts which they regard as derived from the remains of the vitelline duct. MacAuley[7] collected 13 examples of cyst arising from the ileocecal angle and mainly derived from the intestinal mucosa. Multiple cysts near the commencement of the jejunum may be the result of sequestrations from the intestine; Carnot[8] showed experimentally that pieces of mucosa of the stomach and gall-bladder when implanted on the intestine formed cysts, and Walker-Hall[9] described a mesenteric cyst

[1] *Jour. Path. and Bacteriol.*, Edinburgh, 1924, **27**, 1.
[2] *Normandie méd.*, Rouen, 1912,
[3] *Bull. Acad. de méd.*, Paris, 1924, 3c sér., **92**, 1290.
[4] *Brit. Jour. Surg.*, 1924, **12**, 95.
[5] *Rev. de gyn. et de chir. abdom.*, 1912, **19**. 225.
[6] *Rev. de chir.*, Paris, 1904, **29**, 161.
[7] *Brit. Jour. Surg.*, 1923, **11**, 122.
[8] *Arch. de méd. exper. et d'anat. path.*, Paris, 1905, **17**, 273.
[9] *Jour. Path. and Bacteriol.*, Cambridge, 1908, **12**, 128.

lined by gastric mucosa with parietal cells. (*b*) From the remains of the Wolffian body. (*c*) Teratomatous or "dermoid" cysts are infrequent; they may lie between the layers of the mesentery or be attached to its surface and be pedunculated. (2) Serous cysts, lined by endothelium and due to distention of closed peritoneal pouches; they are very rare in the mesentery of the small intestine. (3) Lymphatic cysts may be due to distention of lymphatic vessels or be lymphangiomas, intramesenteric hygromas and then may be congenital; these are Huzella's[1] endothelial cysts. They may contain clear or chylous fluid.

Morbid Anatomy.—Usually unilocular these cysts are occasionally multilocular. The cysts may project from the free border of the intestine or from its mesenteric border and may then pass between the layers of the mesentery, being embedded in the layers of the mesentery without any direct connection with the intestine. They are covered by peritoneum and their walls are composed of fibrous tissue; and may contain smooth muscular fibres very irregularly arranged, and some fat. There may be no layer of epithelium on the interior of the cysts, which may be lined by granulation tissue.

The contents may be clear and serous, containing albumin and cholesterin; turbid, viscid, with mucin; chylous, with the chemical composition of chyle. Timball[2] collected 49 cases of mesenteric cysts with hemorrhagic contents. Turnure[3] has collected 50 cases of gaseous cysts in connection with the intestine; they have been regarded (1) as true neoplasms which secrete gas from the blood, and in this respect comparable with the air bladders of fishes (Mair[4]), (2) as due to bacteria, or (3) as purely mechanical. Skiagraphy shows marked luminosity of the abdomen.

Physical Signs.—The cyst is round, well-defined, tense, elastic, movable, is usually on the right side of the abdomen a little below the umbilicus, and is not connected with any of the viscera except the intestines. It is dull on percussion, is surrounded by resonant intestine, and there may be a band of resonance due to the attached piece of intestine running across it.

Symptoms.—A sudden attack of abdominal pain is usually the first indication of the existence of a mesenteric cyst; there may be recurrent attacks of colic and vomiting; while in a number of the instances acute intestinal obstruction has resulted from kinking of the intestine. On the other hand the symptoms may be those of gastro-enteritis.

Diagnosis is often difficult, and when the cyst is detected, must be made from a distended gall-bladder, hydatid cysts hanging down from the liver or in the peritoneum, floating kidney, ovarian or parovarian cysts of small size with a long pedicle, solid tumors of the mesentery or omentum, pancreatic cysts which are much larger, and even an appendicular abscess. No exploratory tapping is permissible.

Treatment is surgical, and consists in the enucleation of the cyst when this is possible, if not in drainage. These cysts should be operated upon without waiting for urgent symptoms.

[1] *Virchow's Archiv*, 1921, **233**, 260.
[2] *Rev. de chir.*, Paris, 1910, **41**, 45.
[3] *Ann. Surg.*, 1913, **57**, 811.
[4] *Jour. Path. and Bacteriol.*, Cambridge, 1908, **12**, 433.

Omental Cysts.—The omentum may be the seat of cysts of various kinds, such as hydatid and "dermoid," which are referred to elsewhere. Meyer[1] states that 72 cases are on record, and Hasbrouck[2] distinguished (1) true cysts inside the omentum of which he collected 20 examples from (2) cysts attached to the omentum, such as detached ovarian cystadenomas, of which he collected 12. Gairdner,[3] Braithwaite,[4] Mathews[5] and others described large single cysts with clear contents, possibly cystic lymphangiomas. Hemorrhage may take place into these omental cysts; Oberlin[6] collected 23 cases of gangliomous omental cysts, of which 12 appeared to be due to hemorrhage into a serous cyst, 6 encysted hematomas and some cystic tumors; 8 were in children under eleven years of age, and 6 of these were congenital. Some are, like the retroperitoneal cysts, derived from the Wolffian body. Multiple cysts possibly due to lymphatic obstruction have been recorded; Firket[7] believes that proliferation of the peritoneal epithelium may form multiple small cysts. Of 22 cases quoted by Fort,[8] 50 per cent. were under ten years of age, and three-fourths were females.

The condition does not appear ever to have been definitely diagnosed before the abdomen was opened. Symptoms are not prominent in the early stages of growth, and pain usually leads to examination of the abdomen and the detection of a cyst which is superficial in position and usually movable to a limited extent.

Diagnosis.—Lipomas are the only solid tumors likely to be confused with omental cysts. The large omental cysts may imitate localized tuberculous peritonitis, or ovarian cysts with a long pedicle.

Peritoneal Sanguineous Cysts.—Intra-abdominal cysts containing blood may be of various kinds. Thus, hemorrhage may take place into preëxisting cysts, for example, as the result of twisting of the pedicle of an ovarian cystadenoma, or into a mesenteric cyst. Hemorrhage may occur into a soft sarcoma, and malignant hypernephromas may contain more blood than growth. Collections of blood in the female pelvis, which are generally ectopic gestations, ruptured aneurisms, and angiomas, need only be mentioned in order to be distinguished from a fairly definite group of cases, the peritoneal sanguineous cysts (Fisher[9]). Many so-called pancreatic cysts with blood-stained contents are the same as the sanguineous cysts found elsewhere in the peritoneal cavity, and are hemorrhagic effusions into the lesser sac of the peritoneum and therefore peripancreatic, not pancreatic.

Morbid Anatomy.—These cysts may also be found in the great and gastrohepatic omentum, mesentery, mesocolon, or project from the peritoneum lining the back of the abdomen. The writer examined a sanguineous cyst arising in the pelvis in a man. The walls of the cysts are composed of well-formed fibrous tissue and may contain some patches of blood pigment. They are usually lined by adherent shaggy

[1] *Jour. Med. Res.*, 1924, **44**, 401.
[2] *Ann. Surgery*, 1908, **48**, 206.
[3] *Trans. Path. Soc.*, London, 1852, **3**, 374.
[4] *Lancet*, London, 1898, ii, 1472.
[5] *Brit. Med. Jour.*, 1905, ii, 1642.
[6] *Rev. de chir.*, 1921, **59**, 216.
[7] *Arch. de méd. expér. et d'anat. path.*, Paris, 1912, **24**, 697.
[8] *Ann. Surgery*, 1907, **45**, 382.
[9] *Guy's Hosp. Rep.*, 1893, **49**, 274.

fibrin. The fluid is reddish brown and contains blood corpuscles and in some instances cholesterin. In cysts in contact with the pancreas the fluid contains pancreatic ferments. Blood-clot in various stages of change may be found in these cysts. Large nucleated cells—probably endothelial and derived from the peritoneum—also occur in the fluid.

Pathology.—These cysts are probably the result of traumatic hematomas, but as the cyst may not become manifest until some time has elapsed since the injury, it has been suggested that local peritonitis first occurs and later hemorrhage from the newly formed vessels.

Clinical Features.—The cyst is much commoner in the upper than in the lower half of the abdomen, and is usually in the middle line. It forms a large, tense tumor, may have pulsation conducted to it from the aorta and can be shown by percussion to be distinct from the liver. Symptoms are less marked than in pancreatic cysts, and after reaching a considerable size the tumor may remain unaltered for years.

Diagnosis of peritoneal sanguineous cysts other than those around the pancreas is very difficult. This is mainly due to their rarity.

Treatment is surgical and consists in draining the cyst. Excision is rarely possible, as the walls are so often part of the peritoneum forming the mesentery, lesser omentum, or mesocolon. Cure has followed tapping but it is dangerous.

Retroperitoneal hematomas are rare; they may be due to trauma, such as rupture of the kidney, bursting of an abdominal aneurism, or leakage from a hemorrhagic retroperitoneal or renal sarcoma. In some instances the source of the blood is not clear. The blood tracks down behind the peritoneum toward the pelvis, and may form a distinct tumor accompanied by pain. On the right side such a tumor may suggest appendicitis. The symptoms may be those of acute intestinal obstruction.

Embryomas or "dermoid" cysts in rare instances occur in the peritoneum without any evidence that they were derived from the ovaries. Thus, Pakowski[1] collected 74 of these dermoid cysts, 31 of which were connected with the mesentery of the small intestine. These cysts may be simple or composed of skin only, or composite embryomas. They are usually found in females, but Pakowski collected 6 dermoids of the mesentery in males. They may occur between the layers of the mesentery, omentum, and transverse mesocolon, or in the retroperitoneal space. In some instances, however, a "dermoid" cyst originating in the ovary may become detached and subsequently contract adhesions elsewhere. Webb-Johnson[2] found an embryoma attached to the great omentum and to the posterior surface of the urinary bladder by a thin peritoneal fold, which clinically caused symptoms suggesting a calculus in the left ureter. Multiple "dermoid" cysts may be due to rupture of an ovarian embryoma with implantation of fragments over the peritoneum; the multiple growths are not malignant, but resemble the implantations sometimes associated with ovarian papillomas. Suppuration occasionally occurs in these cysts, and in rare instances, of which Montgomery[3] collected 10 cases, the teratomas become malignant.

[1] *Arch. gén. de chir.*, Paris, 1912, **6**, 1029

[2] *Brit. Med. Jour.*, 1925, i, 598.

[3] *Jour. Exper. Med.*, 1898, **3**, 259.

Retroperitoneal Cysts.—Handfield Jones[1] has put forward the following classification on embryological grounds: (*A*) of genito-urinary origin, pronephric, mesonephric, metanephric, and Müllerian; they are more frequent in females between fifteen and twenty-five years of age, and on the left side; (*B*) mesocolic; (*C*) teratomatous; (*D*) lymphatic; (*E*) hemorrhagic from trauma; (*F*) parasitic, hydatid. Cysts manifestly arising in the kidneys, adrenals, and pancreas, are not included in this category. A multilocular cyst, structurally resembling an ovarian cystadenoma, may occur in the retroperitoneal tissues of men as well as of women. These cysts may arise close to the kidney and be mistaken for a floating kidney, a hydronephrosis, or on the left side for a primary neoplasm of the tail of the pancreas. Severe attacks of pain, simulating Dietl's crises or those of appendicitis, may occur. The cysts may pass between the layers of the mesentery, omentum, mesocolon, or mesorectum, and in all probability are derived from sequestrations of the Wolffian body. They may contain several pints of fluid. The multilocular cysts may become malignant and give rise to metastases.

Among rare conditions cystic dilatation of the receptaculum chyli and collection of fluid in a subcecal pouch, the mouth of which has been closed, may be mentioned.

Urachal Cysts.—The urachus may be partially pervious; thus minute cystic dilatations were found in 24 out of 74 cases specially examined by Wutz.[2] In rare cases there are cysts containing many pints of fluid. In some instances the cysts communicate with the bladder; infection may then spread into the cyst; in other instances the cyst and the urinary bladder are connected by an impervious cord. The contents may be clear, turbid, blood-stained, or purulent. The cysts are usually in front of the peritoneum and adherent to the umbilicus and anterior abdominal wall, but may be intraperitoneal; the latter position is explained by a persistence of the fetal mesentery of the urachus. The wall contains smooth muscular, elastic and fibrous tissue, and may show epithelium resembling that of the bladder, but this may be detached. The cysts are usually unilocular, but in Doran's[3] case there were two cysts. Weiser[4] tabulated 89 cases, but included 19 "allantoic" cysts. They occur chiefly in women, but have been met with in men and in children. In Weiser's 89 cases females were about three times more often affected than males. The cysts are in the middle line between the umbilicus and the pubes; they may be soft and fluctuating, resembling a distended urinary bladder, or firm and apparently solid. There may be pain in the lower part of the abdomen, probably from associated local peritonitis. A blood cyst with calcified walls in the subperitoneal tissue was at first regarded as a urachal cyst (Milligan[5]). They may imitate encysted peritonitis, especially of tuberculous origin, and ovarian cystadenomas.

The *treatment* of urachal cysts is surgical. In some instances they can be dissected out, in others the only available course is drainage.

[1] *Brit. Jour. Surg.*, 1924, **12**, 119.
[2] *Virchow's Archiv*, 1883, **92**, 387.
[3] *Medico-Chirurgical Transactions*, London, 1898, **81**, 301.
[4] *Ann. Surg.*, 1906, **44**, 529.
[5] *Proc. Roy. Soc. Med.*, 1924, **18**, (Sect. Urol.), 6.

It is important that the relation of the cyst to the bladder and the possibility of a communication between the two should be borne in mind, otherwise a urinary fistula may follow operation. Tapping the cysts is only a palliative measure, as the fluid is prone to accumulate again.

Conditions Simulating Peritoneal Cysts.—Encysted peritonitis may simulate a true cyst. Kelly and Hurdon[1] figure cysts of this nature adherent to the tip of the vermiform appendix. The "allantoic" cysts described by Lawson Tait[2] and B. Robinson[3] in adult women are probably examples of localized pelvic tuberculous peritonitis (Doran).

Pseudomyxoma of the peritoneum consists in the presence of numerous encysted collections of gelatinous material in the peritoneum, secondary to rupture of an ovarian cystadenoma, or less frequently of a mucocele of the appendix; in some instances, of which Ries[4] reported 2, there is both a rupture of an ovarian cyst and of the vermiform appendix. It may be confused with colloid cancer and with primary tumors derived from the Wolffian body which structurally resemble ovarian cystadenomas.

Malignant Tumors

Malignant growths are more often met with in the peritoneal cavity than innocent tumors, but this depends on the frequency of secondary infection of the peritoneum, for while primary malignant disease and innocent neoplasms of the peritoneum are both rare, primary malignant disease is the more exceptional of the two.

Primary Malignant Diseases.—These may conceivably arise in several structures, such as (1) the endothelium of the serous membrane, of the lymphatics and bloodvessels; (2) the subserous connective tissues, especially around the spine and back of the abdomen, the periosteum of the spinal column and pelvis; and (3) the remains of the Wolffian bodies, Müllerian ducts, accessory adrenal bodies, or even from teratomas that have undergone malignant transformation.

The tumor growth may occupy the omentum or, more rarely, the mesentery or the gastrohepatic omentum, and be thus to all intents and purposes intraperitoneal. In other cases the growth extends behind the peritoneum and to a slight extent displaces the abdominal contents forward; these are cases of retroperitoneal sarcoma. In some instances a growth at first definitely retroperitoneal passes forward, becomes pedunculated, and therefore partly intraperitoneal. Thus, although it might appear to be more logical to describe separately malignant disease (*a*) arising from the peritoneum itself, and (*b*) originating in the tissues (as apart from the organs) of the retroperitoneal space, any such distinction would in reality be artificial.

Morbid Anatomy.—Primary malignant tumors of the peritoneum and retroperitoneal space belong to the group sarcoma or endothelioma. Formerly primary carcinoma of the peritoneum was commonly described; alveolar growths resembling carcinoma histologically undoubtedly occur,

[1] *The Vermiform Appendix and its Diseases*, 1905, 311.
[2] *British Journal of Gynecology*, 1887, **2**, 328.
[3] *Ann. Surg.*, 1891, **14**, 350.
[4] *Surg., Gynec., and Obst.*, 1924, **39**, 569.

but are now regarded as endotheliomas and arising in endothelium, either of a lymphatic or bloodvessel or possibly of the surface of the serous membrane (Miller and Wynn[1]). The histological appearances of primary malignant growths of the peritoneum vary considerably; spindle-celled, round-celled, and irregular-celled, alveolar, fibrifying myxosarcoma and lymphosarcoma, lymphocytoma, endothelioma, and perithelioma (angiosarcoma) all occur. But in 16 primary sarcomas of the omentum 11 were spindle-celled (Bonamy[2]). In some endotheliomas the microscopic appearances are confusing, in some parts resembling carcinoma, in others sarcoma, and are prone to degenerative changes. Crowdy's[3] case was free from these changes and resembled an endothelioma of the pleura.

The shape of the tumors varies according to their position. Retroperitoneal sarcoma and neoplasms originating between the layers of the great omentum are often flattened out so as to resemble a pancake. Retroperitoneal sarcomas may project forward into the peritoneal cavity and even become pedunculated. There may be multiple pedunculated growths without any manifest primary growth. A primary malignant growth of the peritoneum may be rounded or lobulated. The tumors may reach a considerable size. The origin of primary malignant neoplasms is more rarely intraperitoneal than retroperitoneal. This depends on the presence behind the peritoneum of structures, such as lymphatic glands, connective tissue, and the remains of the Wolffian body and Müllerian duct, from which tumors may arise. As a rule, primary peritoneal and retroperitoneal tumors do not invade adjacent organs to any great degree. It may, however, be difficult to determine the exact origin of a malignant growth, and in some instances it must be left an open question whether the growth arose in an organ and spread out of it or whether it started independently of a given viscus and subsequently infiltrated it. In such cases the histological appearance of the tumor is the best guide to its origin.

The lymphatic glands and the connective tissues around the aorta and the periosteum of the vertebræ appear to be the commonest starting-points of retroperitoneal sarcoma. A malignant cystic tumor resembling an ovarian cystadenoma, and probably derived from the remains of the Wolffian body, may occur.

Retroperitoneal sarcoma most often arises in the lumbar region and more frequently on the right side, but it may start in the middle line, in the iliac region, or in rare instances in the pelvis. There is frequently some local peritonitis with adhesions over the growth. The tumor is usually firm at first, but in a third of the cases it undergoes central necrosis and becomes cystic (Dutton Steele[4]). The contents may be hemorrhagic, myxomatous or purulent from infection. The pseudocyst has in rare instances opened into the intestine or peritoneum. Thus in a case under my care, a cystic, spindle-celled sarcoma arising near the

[1] *Jour. Path. and Bacteriol.*, Cambridge, 1908, **12**, 267.
[2] *Rev. de gynéc.*, Paris, 1908, **12**, 285.
[3] *Surg., Gynec., and Obst.*, 1925, **40**, 196.
[4] *Am. Jour. Med. Sci.*, 1900, **99**, 311, and 1904, **127**, 939.

right kidney opened into the duodenum. The growth may press on the inferior vena cava, the spinal nerves, or on the abdominal viscera. The fixed parts of the colon are more liable to be narrowed by retroperitoneal growths. Tumors in the omentum, which may become cystic, may constrict the colon, and in primary sarcoma of the gastrohepatic omentum, of which Cobb[1] has been able to collect three examples only, the stomach may be depressed downward (A. P. Gould[2]). Secondary growths occur in 33 per cent. of the cases, and are found in the liver, lungs, and peritoneum, and may give rise to ascites.

Etiology.—Sex apparently has no influence. In retroperitoneal sarcoma, according to Dutton Steele, the first, fourth, fifth, and sixth decades are most often affected, and 53 per cent. occur between thirty and sixty years of age. Injury has been thought to be a causal factor.

Clinical Picture.—The clinical manifestations vary considerably; most commonly there is a deep-seated abdominal tumor with somewhat variable gastro-intestinal symptoms, abdominal distention, and increasing weakness. Although usually fixed, the tumor is occasionally freely movable, especially in the early stages. It may be regular and smooth, or nodular, more or less firm, or may show various degrees of consistency; it may receive transmitted pulsation from the aorta; it is usually not tender on palpation, and is more often to the right of the middle line; a growth in the omentum may resemble a spleen dislocated by extensive deformity of the spine. Primary growths, especially in the omentum, may induce ascites and so imitate tuberculous peritonitis, while a flat retroperitoneal sarcoma, although not palpable, may by pressure on the spinal nerves give rise to severe pain in the back imitating that of aneurism, caries, or malignant disease of the spine, and by compressing the inferior vena cava lead to œdema of the legs, genitals, and lower part of the abdomen with very noticeable enlargement of the subcutaneous abdominal veins. There may be profound anemia before any tumor is palpable. On the other hand, malignant disease of the omentum may produce a large superficial mass forming a kind of shield in front of the intestines or may simulate enlargement of the liver.

The progressive growth of the tumor usually causes pain and sometimes vomiting, constipation, and even intestinal obstruction. The sudden onset of abdominal pain, probably due to extension of the growth setting up local peritonitis, may be the first symptom. The growth may then be sufficiently large to be easily detected. Although the tumor may be of considerable size, the general state of nutrition is less affected than in malignant growths of the stomach or liver of the same dimensions. When retroperitoneal it may be resonant from the presence of intestines, colon, or stomach in front of it. When ascites is present the fluid may be but is not necessarily blood-stained. It may be chylous or remarkably viscid from the presence of a "mucoid" body. The course is somewhat rapid, the average duration of retroperitoneal sarcoma from the onset of symptoms being eight and a half months (Dutton Steele). Death is usually due to exhaustion, but in a few instances has been

[1] *Annals of Surgery*, 1906, **44**, 16.
[2] *Medico-Chirurgical Transactions*, London, 1900, **83**, 257.

sudden and due to rupture of the growth and hemorrhage into the peritoneal cavity.

Diagnosis.—From the variable character of the symptoms this is very difficult and is usually arrived at only by a process of exclusion. Even although a peritoneal tumor be diagnosed, it is, except when there is definite evidence of other growths, impossible to be absolutely certain that it is malignant unless the abdomen has been opened. Even then removal of a piece of the growth for histological examination is necessary to be absolutely certain, for in a considerable number of cases the abdomen has been opened and closed on the discovery of an inoperable and apparently malignant tumor, and yet the tumor has subsequently disappeared (Greig Smith[1]). These "vanishing tumors" (Power[2]) may possibly be inflammatory in nature; in some instances a foreign body which has perforated the intestine may be the cause (Bland-Sutton[3]), and in some the condition may be due to actinomycosis or pancreatitis (Bradford[4]). Malignant growths progress more rapidly, produce more marked constitutional symptoms, and give rise to pressure symptoms, such as pain and dilated abdominal veins, in a far greater degree than innocent tumors even though of great size. The differential diagnosis must be made from various conditions, such as pancreatic cysts, renal and suprarenal tumors, malignant disease of the liver, aneurism of the abdominal aorta which does not pulsate, retroperitoneal teratomas and innocent tumors, some cases of carcinoma of the colon with suppuration, uterine fibromyomas, and when there is ascites from secondary malignant disease of the peritoneum and from tuberculous peritonitis. A horseshoe kidney, which is met with once in 1600 autopsies, has been mistaken for malignant disease. A nodular mass may resemble fecal accumulation, and enemas and purgatives may then be necessary to settle the diagnosis.

Prognosis is extremely grave. Operative interference is impracticable in many cases, especially in extensive retroperitoneal sarcomas. Tumors in the omentum or mesentery are more amenable to removal. Removal of the tumor in an early stage, when it is more or less encapsulated, should lead to better results. In Williams'[5] collection of 84 cases of retroperitoneal sarcoma, radical operations were performed in 12 cases, with recovery in 10.

Treatment.—Except when removal is possible, treatment is palliative and symptomatic.

Secondary Malignant Disease of the Peritoneum.—Synonym: Malignant peritonitis. Secondary infection with carcinoma or sarcoma is far commoner than primary malignant disease of the peritoneum. That it occurs more frequently in women is in part accounted for by influence exerted by malignant disease of the sexual organs, mammæ and gall-bladder. It chiefly occurs in or after middle life.

Pathology.—The primary growth is usually in the abdominal organs. Malignant infection may also extend from the chest, either through the

[1] *Medico-Chirurgical Transactions*, London, 1894, **77**, 139.
[2] *Lancet*, London, 1899, i, 583.
[3] *Ibid.*, 1903, ii, 1148.
[4] *Clin. Jour.*, London, 1907, **21**, 76.
[5] *Am. Jour. Med. Sci.*, 1903, **126**, 269.

lymphatics of the deep fascia of the parietes from the mamma, described by Handley[1] as "epigastric invasion" of the peritoneum, or less commonly from the cavity of the thorax as in primary carcinoma of the œsophagus. In primary malignant disease of the testes the lumbar glands may convey infection to the peritoneum. In some instances, as in generalized sarcoma, infection reaches the peritoneum by the blood-stream. Primary malignant disease inside the abdomen may spread to some extent by the lymphatics and bloodvessels, or to a limited degree by direct contact. But the chief means of dissemination is the liberation of infective cells, which become widely scattered over the abdominal cavity.

Morbid Anatomy.—The tumors may be so minute and discrete as to imitate tuberculous peritonitis, and the condition may then be spoken of as miliary carcinomatosis; in other instances the secondary nodules, being larger and white in color, resemble caseous tubercles, while in some cases, especially of colloid carcinoma, the masses are very large indeed. In women the ovaries may become markedly infiltrated with secondary growth, and as they may form tumors much larger than the primary growth, this sometimes suggests that the original tumor growth started in both ovaries (Bland-Sutton[2]). The miliary growths are less translucent than miliary tubercles, when larger they are, as a rule, white, although they may be hemorrhagic, but they do not caseate and soften. The growths, which are generally sessile or more rarely pedunculated, may be umbilicated. The whole of the peritoneum may be infected, but the omentum, the mesentery, and Douglas' pouch are the regions most frequently affected. When the growths are miliary the peritoneum may be otherwise normal, but in most cases the peritoneum shows chronic fibrotic changes resembling tuberculous peritonitis, the white nodules being surrounded with fibrotic thickening and often outlined by a rim of pigmentation. From the resulting contraction the omentum may become rolled up and the mesentery markedly shortened. The intestinal tract may be much shortened, the intestinal walls thickened, and the lumen narrowed. The diaphragm may be much thickened from growth, and in these cases miliary carcinomatosis of the pleuræ with effusion may result. Adhesions may give rise to loculated ascites. In some instances acute or subacute peritonitis is found at autopsy. From implication of the receptaculum chyli or of the thoracic duct the lacteals may be dilated, and from leakage true chylous ascites result; chyliform ascites is commoner.

Occasionally large colloid growths are met with. More than one condition has been described as "colloid cancer" of the peritoneum; secondary growths due to a primary carcinoma of the stomach or colon are occasionally seen, but some of the cases formerly described as colloid cancer are probably primary retroperitoneal growths derived from the Wolffian bodies and are myxosarcomatous or endotheliomatous in nature. The histological character of the tumors will vary with that of the primary growth, spheroidal-celled carcinoma being the commonest form.

Symptoms.—These come on gradually with loss of vigor, flesh, and appetite, and, except that they point to the abdomen, are somewhat

[1] *Lancet*, London, 1905, i, 1047.

[2] *Ibid.*, 1907, i, 1342.

indefinite. The symptoms vary since they are partly due to the primary growth, which is also usually in the abdomen, and partly to the peritoneal metastases; in fact, it is usually impossible to assign the symptoms exclusively to one or other cause. In addition to the progressive wasting and weakness there may be varying degrees of abdominal tenderness. Pain, on the one hand, may be almost absent, or, on the other hand, there may be colic from obstruction to the lumen of the colon, induced either by a primary carcinoma or by pressure or contraction exerted by secondary growths in the neighborhood. Tenderness and pain may be due to attacks of local peritonitis in connection with the growths.

Physical Signs.—In most cases there is ascites which may obscure the existence of any growths. The fluid may be clear, turbid, blood-stained, chylous, or pseudochylous. The abdomen may be much distended. There may be prominent veins under the skin of the abdominal wall. The umbilicus may be infiltrated with secondary growth, and small nodules may be felt in the line of the falciform ligament; it should be remembered, however, that small masses of fat in this position may imitate nodules of secondary growth. As the result of distention the skin of the abdomen shows lineæ albicantes. Even when not previously stretched the skin may from loss of its elasticity be thrown into numerous wrinkles and become somewhat harsh and rough.

Although there is usually emaciation, and to a greater degree than in primary malignant disease of the peritoneum, there is sometimes a very considerable amount of subcutaneous fat. Cutaneous pigmentation is not uncommon; and in very rare instances the skin of the abdomen shows a warty pigmented condition called acanthosis nigricans. Œdema of the feet, which may creep up the thighs to the abdomen, may be due to pressure on the inferior vena cava, or in the later stages depend on cardiac weakness. In some cases definite tumors can be felt through the abdominal wall; very frequently the omentum is rolled up and palpable as a hard tumor or transverse ridge, which must not be mistaken for the lower margin of the liver. There may be friction over the tumors. Often when ascites is considerable no growths can be detected until the abdomen has been tapped, and when the growths are small nothing may be felt even then. There may be concomitant pleural effusion on one or both sides due to intrathoracic infection. The duration of the disease is seldom more than six months and is often much less.

Diagnosis.—When definite tumors can be felt in a patient who has malignant disease of the stomach, colon, etc., there can be no doubt. When tumors are palpable, but there is no history or definite evidence of malignant disease, the diagnosis must be made from tuberculous peritonitis, from fecal accumulation, and from the rather rare condition of multiple hydatids in the peritoneum. Tuberculous peritonitis is commoner in children and women, and may be accompanied by fever and by signs of suppuration about the umbilicus, while injection of the ascitic fluid into guinea-pigs would provide evidence of tuberculosis. The use of tuberculin is another means of diagnosis. A blood-stained effusion is in favor of malignant disease. The discovery of multiple tumors in the abdomen should always suggest the possibility of fecal

accumulation, and the effects of purgatives and repeated enemas should be tested. Multiple echinococcus cysts in the abdominal cavity run a slow course as contrasted with malignant disease, and may be definitely recognizable as cysts, while the history of a hydatid cyst in the liver makes the diagnosis of a similar condition in the peritoneum highly probable. In cases with marked ascites the presence or absence of tumors cannot be settled, and it may be impossible to decide whether the underlying condition is malignant disease or hepatic cirrhosis, simple chronic peritonitis, and other causes of ascites, such as portal thrombosis, until the abdomen is tapped. The malignant growths in the peritoneum may be too small to be felt. In these cases enlarged glands in the groins or above the left clavicle, and to a lesser degree of a blood-stained ascites, indicate malignant disease. For cytological diagnosis, see p. 904.

Prognosis is, of course, hopeless.

Treatment is purely palliative and in the direction of the relief of pain by opium, morphine, and external applications to the abdomen, in the alleviation of gastro-intestinal symptoms, and the removal of ascitic fluid by tapping. To prevent reaccumulation of fluid after tapping, the injection of a dram of adrenin (1 to 1000) diluted with water to half an ounce may be tried.

CHAPTER XV

SPLANCHNOPTOSIS. VISCEROPTOSIS. ENTEROPTOSIS. GLÉNARD'S DISEASE

By THOMAS R. BROWN, M.D.

The word enteroptosis, although in reality meaning a falling or descension of the intestines, has been generally used to signify the descent of any or all of the abdominal viscera. The better word is splanchnoptosis. In describing the displacement of the individual organs special terms are used, such as nephroptosis, to signify descent of the kidney; gastroptosis, of the stomach; splenoptosis, of the spleen; hepatoptosis, of the liver; coloptosis, of the colon; while some use the term enteroptosis to mean descent of the intestines. The condition may be partial or universal, and the different organs may be affected in varying degrees. It is also known as Glénard's disease, from the physician who first described it carefully. Etymologically speaking, all the terms are incorrect, and we should use nephroptosia, gastroptosia, etc., as A. Rose specially insisted.

One thing must be remembered in the discussion of this condition, and that is, that in the earlier days nephroptosis, being much more easily recognized, was regarded as the most important feature, and to it were ascribed the protean symptoms often met with, while later investigations with better methods of diagnosis have shown that the displacement of the kidneys is usually associated with the displacement of the stomach, intestines, etc., and that many of the symptoms originally ascribed to floating kidney are referable to displacement of other organs.

Anatomy and Embryology.—Before discussing the etiology of splanchnoptosis it will be advisable to call attention briefly to the anatomy and embryology of the abdominal organs. These viscera are held in their positions by a number of different forces: by the negative pressure of the thoracic cavity acting through the diaphragm; by ligamentous, vascular and peritoneal attachments; by the intra-abdominal fat; by the pressure of other abdominal organs; and by the supporting power of the abdominal muscles. Physiologically, no organ is absolutely fixed, but each is capable of a slight degree of movement, which may be caused by various factors, such as the position of the patient, the amount of food ingested, the passage of urine and feces, the respiratory and circulatory movements, and pregnancy. Thus we must not consider the abdomen to be filled with viscera that are normally fixed in their positions, but rather of organs capable of a slight degree of movement under a variety of conditions, the only fixed area in the abdomen being the radix mesenterica.

Embryologically the subject is interesting because of the fact that a number of authors regard splanchnoptosis as a reversion of the abdominal

organs to the embryonic type, as Rosengart and Henle have shown. From the fetal position of the viscera the position found in normal children and adults is produced by gradual ascension of the various viscera, this being largely due to the fact that after respiration the liver rotates and rises into the dome of the diaphragm, and also undergoes a relative diminution in size. In advanced cases of splanchnoptosis the position of the abdominal organs very closely resembles that seen during embryonic life.

Pathogenesis.—As regards the pathogenesis of splanchnoptosis divergent views are held, some believing that the condition is congenital, others that it is acquired, while others hold a middle ground. According to Glénard, the starting-point of the condition is the falling of the right colic flexure, due to a weakening of the hepatocolic ligament. This may follow injuries, pregnancies, strains, dyspepsia, typhoid fever, appendicitis, or localized peritonitis, but is primarily due to a constitutional defect as regards the strength and supporting power of the mesenteric tissues which is present in certain individuals.

Stiller is another firm adherent of the *congenital* origin of splanchnoptosis, and he believes that this inherited tendency is shown by a constant organic type, a slender skeleton, a long thorax, soft, flabby muscles, and a diminution of the panniculus adiposus, and that in these patients may be found a neurasthenic stigma, the floating tenth rib. According to him the basis of the disease rests upon an embryological defect, and the numerous assigned causes are not primary causes, but simply factors which bring about a condition to which the body is embryologically committed. Fuhs is a firm believer in the costal stigma, and calls attention to the frequency of splanchnoptosis among young unmarried Swedish girls who have never worn corsets and who have strong abdominal walls. The condition is found frequently among Arab women, who wear no constricting articles of clothing. Mathes believes that splanchnoptosis is a constitutional and hereditary anomaly of the entire organism, a lack of vital energy of all the vital tissues, while Harris believes that it occurs in women with a particular body form, which can be expressed mathematically in terms of certain body diameters, and that practically all women with this body form have movable kidneys to some extent.

Landau believes that the primary cause is a weakness of the abdominal wall, in many cases congenital, while according to Bouveret, neurasthenia is primary, splanchnoptosis secondary. Rosengart believes that in many cases there may be a real persistence of the fetal condition. Riegel, on the other hand, is a firm believer in the acquired nature of the disease, and thinks that any condition which either increases the pressure above the diaphragm or diminishes the pressure below may produce splanchnoptosis, such as pregnancy and parturition, wasting diseases, and the removal of abdominal tumors or ascitic fluid.

Wolkow and Delitzen have carried out a number of interesting experiments in regard to the production of nephroptosis, and they conclude that the use of a belt may dislocate the kidney downward, may fix it, or may even move it upward according to the position of the belt. According to these investigators, nephroptosis is an infallible index of an existing

alteration of the intra-abdominal equilibrium. Janovski, from his experimental studies, thoroughly agrees with these conclusions, while Longyear believes that the ligamentous union of kidney and colon is an even more important factor in the etiology of nephroptosis.

Victor believes that "the fundamental cause of splanchnoptosis is abdominal incompetence, which is a developmental factor. Failures in the normal development of abdominal competence and visceral retention are correlated with the development of certain departures from the normal body form—the most constant being the retracted lower thorax. Variations in these developmental processes ('normal,' or retarded, or uncompleted, or reversive) may be observed in continual operation in all human beings, and the pictorial and plastic history of the race shows them to have been occurring ever since such history began."

Quincke gave three causes of splanchnoptosis: (1) Relaxation or stretching of the abdominal wall; (2) change in the form of the abdominal cavity; (3) stretching of one or more of the suspending ligaments; while Langerhans recognizes five causes: (1) Relaxation of the abdominal muscles; (2) hereditary predisposition; (3) pressure of clothing, as tight belts and corsets; (4) chlorosis; (5) nervous dyspepsia.

The most valuable contribution to the pathogenesis of splanchnoptosis is that of Keith, who believes that the condition is the result of a vitiated method of respiration. According to him the organs within the thoracic and abdominal cavities are poised between the muscles of inspiration and expiration, two contending sets, which throughout the life of the individual strive for the mastery. The reason that the right kidney is so much more frequently displaced than the left is because the liver acts directly on the former, while in the case of the latter there is a safety valve in the shape of the splenic flexure of the colon, which may enter or leave the hypochondrium with the greatest freedom; also the left kidney is bound to the spleen, and the fundus of the stomach represents a much lighter hammer than the liver. The adhesion of the base of the pericardium to the diaphragm, peculiar to man and the anthropoids, is a most effective aid against ptosis. Briefly speaking, Keith's conclusions are as follows: (1) The contraction of the diaphragm is the factor which produces the displacement of the viscera in splanchnoptosis or Glénard's disease, and further, that of the various parts of the muscle, the crura are the most important agents in producing this result. (2) Before the displacement can be produced, either what he terms the thoracic supports of the diaphragm must have yielded, or the antagonistic abdominal muscles must have been hampered or weakened in their action, as, for example, by tight corsets. (3) The bonds which fix the viscera to the walls of the abdomen are of quite subsidiary importance.

Thus the theories regarding the pathogenesis of splanchnoptosis may be broadly placed in three groups: (1) The condition is congenital, and is due to an inherent weakness of the tissues which support the abdominal viscera; such factors as clothing, trauma, disease, etc., are not primary but simply contributory causes, which bring out or accentuate the inherited tendencies. (2) The condition is due to a number of causes, each of which has as its result the weakening of the various

visceral supports, due in some cases to pressure, in other cases to adhesions, in other cases to trauma, and in still other cases to a marked diminution of the supporting power of the abdominal wall. (3) Each of the foregoing may be the primary cause; in other words, there may be both an acquired and a congenital form of splanchnoptosis.

In the great majority of instances, according to personal observations, the condition is due to a congenital defect, yet in some it may definitely be of the acquired type.

Frequency.—In discussing this we necessarily quote the frequency of displaced kidney; displaced stomach, etc., because in the vast majority the descension of one organ is associated with that of other organs, although for various reasons the one organ alone has been considered. Naturally the only tables of value are those of recent years, when the condition has been well recognized, and when clinicians have been on the alert to diagnose it. Lawson Tait stated that there were no movable kidneys, and yet we have but to look at many older pictures, notably Botticelli's women and Memling's Eve, to realize that the condition has unquestionably been present for a long time, although it is highly probable that it is on the increase. The condition has been found in practically all the races in which it has been carefully looked for.

Glénard reported 148 among 1310 patients at Vichy; Stiller meets from 300 to 400 cases of splanchnoptosis in his private practice every year; while Kuttner found 100 cases of this condition among 4000 patients in Ewald's clinic; Kuttner also states that he frequently found floating kidneys in children, which is also the writer's experience and that of Blum. Einhorn in one year saw 70 cases of splanchnoptosis among 1080 males, and 277 cases among 832 females. Of 240 cases of enteroptosis proper, 20 were in men and 220 in women, and in these cases movable kidney was met in 212, movable liver in association with movable kidney in 23 cases, and in 12 patients without movable kidney. Enteroptosis alone was met with in 15 patients, 1 male and 14 females, and movable kidney alone 57 times, 21 males and 36 females. Thus in Einhorn's practice, which is largely devoted to digestive disorders, and in which, therefore, the figures are extremely high, ptoses of the abdominal viscera are met with in 6.5 per cent. of the males and 33.25 per cent. of the females.

Movable Kidney.—As regards its incidence the older anatomists and clinicians noted it but rarely; thus, Ebstein found movable kidney only 5 times in 3658 postmortems, while Landau reports only 4 cases among 6999 hospital patients. Later reports, however, show the great incidence of this condition, especially among women; thus, Lindner found that one out of every four women had displaced kidney; Mathieu found 85 cases among 306 patients; Larabee reports 112 cases among 272 patients in the Out-patient Department of the Boston City Hospital; Glénard, in his statistics published in 1893, found 481 cases of floating kidney among 3788 patients, 2.7 per cent. in men and 22 per cent. in women; Wolkow and Delitzen found 66 cases among 221 women; Einhorn found nephroptosis in 1.81 per cent. of males and 20.6 per cent. of females. According to Burnam, who investigated the records of the Johns Hopkins

Hospital, one of every 5 women had a movable kidney, and one out of every 50 men, these figures agreeing absolutely with those of Tuffier.

As regards the grade of displacement, Glénard describes four degrees: (1) When the lower portion of the kidney can be felt only during deep inspiration; (2) when the greater portion of the kidney can be felt, but the upper border cannot be made out; (3) when the whole kidney can be palpated during deep expiration; and (4) when the entire kidney can be palpated, and is capable of being moved about the abdominal cavity, this latter being the true floating kidney. According to Ewald and Kuttner, the degrees of displacement are: (1) The kidney shows a demonstrable respiratory movement without being dislocated to any extent; (2) the kidney shows a dislocation of the first degree, that is, we are able to palpate from one-third to two-thirds of the organ, which can be moved by means of the hand, and is more or less dislocated forward; (3) the kidney shows a dislocation of the second degree, that is, is palpable over its entire extent, is easily moved by the hands and during respiration, and lies near the anterior abdominal wall, or, at least, is easily brought there; and (4) the kidney is dislocated and fixed in an abnormal position. In Kuttner's and Ewald's series of 79 cases associated either with dilatation or displacement of the stomach, in 47 the right kidney was displaced, in 7 the left kidney, and in 25 both kidneys; 18 cases fell under the first grouping, 64 under the second, 19 under the third, and 3 under the fourth.

As regards *age*, displaced kidney, as well as ptoses of the other viscera, is frequently met with in very young children, in several cases under three years of age. In Kuttner's series of 326 cases, 6 were found between one and ten years, 32 between ten and twenty, 82 between twenty and thirty, 123 between thirty and forty, 49 between forty and fifty, 26 between fifty and sixty, and 8 between sixty and seventy; that is, the great majority of these patients when seen by the physician for the first time are between twenty and fifty years of age. Blum has recorded many cases among children, and we have noted the condition frequently in very young infants.

As to the relation of *pregnancy* to floating kidney, in Kuttner's series of 94 patients, 40 had never borne children, 10 had borne one child each, and 44 had borne two or more children each. In Landau's series, 31 of 34, on whom notes were made, had borne no children, while in Lindner's series of 75 patients, 24 had never been pregnant, 12 had been pregnant once, 30 had been pregnant two or more times, while of the others no notes were to be found. Of Drummond's 27 women patients, 16 had borne children, while of Larrabee's 112 cases, 51 were nulliparous and 50 multiparous.

As regards the frequency with which right, left, and both kidneys are affected, in Kuttner's series of 727 cases, in 553 the right kidney alone was movable, in 81 the left kidney alone, and in 93 both kidneys. In Einhorn's series the right kidney alone was movable in 77.3 per cent. of the cases, the left kidney alone in 2.1 per cent., and both kidneys in 20.6 per cent.

Gastroptosis.—As regards its incidence, figures are of little value because, in the first place, the condition is generally overlooked unless associated with gastrectasis or unless special examination is made for it, and in the second place because many of the symptoms, which in reality are due to a displacement of the stomach, have been ascribed to displacement of the kidney. Kuttner and Ewald report 100 cases of displaced kidney, 94 in women, 6 in men, in 79 of which there was either a dilatation or displacement of the stomach. The writer's experience has been that in almost all the cases of splanchnoptosis the stomach is involved to a greater or less extent. The subject is still somewhat undecided because of the great difference of opinion as to the normal position of the stomach.

The radiological observations of Hurst, Alvarez and others seem to show that in many absolutely healthy individuals the position of the stomach is lower than hitherto regarded as normal, and that we must revise our views as to what really constitutes gastroptosis; thus while a high transverse is the rule in the herbivor type of individual, a low vertical is equally natural to the carnivor type.

Glénard has reported 51 cases of *displaced liver*, 32 being associated with movable kidney, and of these, 30 were women and 2 men. Einhorn reports 21 cases of displaced liver in 369 women, 9 cases in 439 men; a moderate degree of abdominal flaccidity was present in 16 of the 21 women. Graham has collected 68 cases of displaced liver, 55 in women, 13 in men, and Savelieff collected 118 cases from the literature.

Several isolated cases of *floating spleen* have been reported, although, unless the spleen is markedly displaced, a ptosis is difficult to determine, because of its position, which can only be determined by the most careful percussion and because of the absence of symptoms. The displacement of the pancreas is of interest because Glénard's *corde colique transverse*, which he believed to be the constricted transverse colon, Ewald regards as the pancreas.

Cardioptosis, or the descension of the heart, Einhorn found 22 times in 926 patients, 18 men, 4 women, and in about one-half of these cases there was an associated hepatoptosis. He thinks the condition is probably due to the downward displacement of the diaphragm. Abnormal position of the œsophagus and cardiospasm have been noted in a certain number of cases of gastroptosis.

The association of displacements of the pelvic organs with splanchnoptosis is a subject to which very little attention has been paid, and yet it is of extreme importance, because retroflexion of the uterus is a very frequent accompaniment of displacement of various abdominal organs. Smithwick found that of 34 women with splanchnoptosis, 80 per cent. had retroversion of the uterus, generally in a marked degree.

A weakened perineal floor due to a relaxed vaginal outlet is unquestionably a contributory factor of importance in the visceroptosis so frequently seen in married women after several pregnancies.

Symptoms.—We will discuss the symptomatology of splanchnoptosis in general, and later call attention to the symptoms especially referable to each of the displaced organs. In the first place, it must be insisted upon that there may be absolutely no symptoms whatsoever, and, in

the second place, that the intensity of the general symptoms does not, as a rule, depend so much upon the extent of the displacement of the various viscera as upon the degree the nervous system is involved. We must not forget that all of these symptoms have been ascribed in turn to each of the viscera, according to whether kidney, stomach, liver, or intestines were the special object of study, and yet in the vast majority the symptoms are referable to a displacement of all or most of the viscera, although the degree of displacement may be different. The usual picture of a patient who presents symptoms is that of a thin, pale, young woman or man of slight build, with dyspeptic and nervous complaints, a nervous expression, and thin, soft abdominal walls in which there is a marked lack of tone. Some have called attention especially to the juvenile expression of the face, others to the fact that the picture closely resembles that met with in phthisis. We may have symptoms of the most aggravated type of psychasthenia or *neurasthenia*, to which are added various abdominal symptoms, such as indigestion, constipation, pain in various portions of the abdomen, a feeling of lack of abdominal support, frequent, sometimes painful, urination, backache, sideache, various respiratory symptoms, cardialgia, pain during or after meals, sometimes nausea and vomiting. All of these symptoms are aggravated by standing, walking, or exercise, while the prone position causes them to markedly diminish and sometimes to disappear for the time being. It is also noteworthy that the symptoms become less if the lower abdomen is lifted up either by an artificial support or by the hands of the physician as he stands behind the patient, or after elevation of the foot of the bed. The greater the congenital anomaly, and the earlier the adjuvant factors act upon one so predisposed, the sooner these symptoms make their appearance. Among the more important objective symptoms may be mentioned a flattened abdomen, often with hypoplastic walls, a bent spinal column, sometimes an abdomen flattened in the epigastric region but distended below the level of the umbilicus; sensitiveness to pressure near the tenth rib in some cases, a cord-like transverse colon (or displaced pancreas, according to Ewald), through which the pulsation of the aorta can be distinctly felt; while in some cases visible swellings can be seen in abnormal locations due to displacement of the various viscera.

Glénard divided the symptoms into three special groups: *hypostasis*, or lack of tone of the abdominal walls, *splanchnoptosis*, and *enterostenosis*. The first shows three special symptoms; deformity of the abdomen, flabbiness of the abdominal walls, and the ease with which the hypochondrium can be compressed. *Splanchnoptosis* shows four special signs: splashing sounds in the stomach, epigastric pulsation, floating kidney, and ptosis of the transverse colon. *Enterostenosis* has three special signs: a palpable contracted band of the transverse colon, of the cecum, and of the sigmoid flexure.

Other symptoms of the most protean character have been ascribed to this condition. Meinert believes that chlorosis in young girls is sometimes a crisis of splanchnoptosis, while Quincke laid stress upon the respiratory symptoms, such as shortness of breath on standing or after exertion, cardiac oppression or distress, and sometimes dizziness or weakness.

Glénard himself described four forms of splanchnoptosis, the gastro-intestinal, the lithemic or hepatic, the neurasthenic, and the cachectic, and believes that in many cases the patient goes from one form into the other in the order named. Keith calls special attention to the frequency with which cervical curvature or ewe-neck is met. He believes that from a clinical point of view the most important of the visceral bands is the gastrohepatic omentum, and that more than half the results of ptosis of the liver and stomach are due to compression, straining or distortion of the bile, blood, nerve and lymph channels in this omentum, and that gall-stones are common in cases of splanchnoptosis.

As to the relationship between neurasthenia and splanchnoptosis, there is a marked difference in opinion, some holding that neurasthenia is primary and splanchoptosis is secondary, others the reverse, while a third group holds, and probably rightly, that in most cases each represents a congenital fragility of tissue independent primarily of each other, but frequently associated and reacting very deleteriously upon each other. Certainly visceroptosis with its gastric atony and intestinal stasis, and the psychasthenic-neurasthenic condition with its increased affectivity and irritability, are the main components of the "chronic intestinal invalid."

It must strike our gynecological brethren that the symptoms which they have ascribed to retroflexion of the uterus bear a striking resemblance to those of splanchnoptosis, and this accentuates the fact that in the vast majority of cases retroposition and retroflexion of the uterus are but associated signs of a general splanchnoptosis, and to expect relief by a ventral fixation of the uterus seems chimerical.

Gastroptosis.—Gastroptosis is one of the most important of the ptoses as regards symptomatology. Undoubtedly many of the symptoms referred to displacement of kidney or liver are in reality due to an unrecognized displacement of the stomach. As to its frequency, it is being more and more recognized as it is more carefully investigated and the roentgen-ray—radiographic or fluoroscopic—furnishes us an easy means of diagnosis, although there is still a considerable divergence of opinion to what is exactly the normal position of the stomach, and how low the most dependent position must be to warrant us in making a diagnosis of gastroptosis. It has seemed to the writer that any stomach that, in the upright position of the patient, reaches below the iliac crests should be regarded as abnormally low in position. Meinert finds displacement of the stomach in 80 per cent. of the patients in his gynecological clinic, while Thompson finds it six times more common in women than in men.

In the downward dislocation of the stomach we have two main forms: First, the whole stomach may be dislocated downward, and second, the stomach may occupy a more vertical position, although, strictly speaking, the former is rare, due to the firm fixation of the cardiac end. The most frequent form is the subvertical, the next is the vertical, while the loop, crescent, or garland form is less common. The vertical or subvertical forms are peculiarly liable to dilatation, this being aided by a general weakness of the patient, frequent overloading of the stomach, relaxation of the abdominal wall, pregnancy and parturition, rapid loss

of weight, and constriction due to corsets. As regards symptoms, there may be none whatsoever; in fact, the symptoms directly referable to the stomach are largely dependent upon the associated atony and motor or secretory anomalies. Steele and Francine found some dilatation of the pyloric extremity in each of 70 patients examined by them. We must, therefore, regard the symptoms met with in gastroptosis as largely due either to a perversion of the motor or the secretory powers of the stomach, or to a dilatation with its characteristic symptoms due to the retention and decomposition of food. If the ptosis is marked, it is hard to see how it is possible to prevent difficulty in the propulsion of food, leading to subsequent distention and atony. So long as the stomach is not overtaxed there is little or no distress, for if the ptosis is not great the stomach is easily able to perform the additional amount of labor. If, on the other hand, excessive work is thrown on the stomach, as after very large meals, rapid eating, the ingestion of much easily fermenting food, the upright position after eating, or eating while greatly fatigued or under mental strain, the stomach is unable to do the excess of work, and atony and possible dilatation occur.

The *symptoms* especially referable to displacement of the stomach are distress and flatulence after meals, sometimes nausea and vomiting, tachycardia, dyspnœa, anorexia, coated tongue, numbness and dizziness, pain, and a feeling of lack of support, while in some cases the dread of gastric disturbances leads to slow starvation and cachexia. Many of these symptoms are in the main due to the associated dilatation or motor insufficiency, while in all cases the quantity of food seems to be of more importance than its quality in the production of symptoms. Rose believes that the condition is identical with atonia gastrica. A splashing or a rumbling sound in the stomach is frequently heard. In many cases the symptoms are more referable to the neurasthenia so frequently associated than to the displacement of the organ *per se*. In gastroptosis, as in the other ptoses, the symptoms are usually lessened by the prone and increased by the upright position.

As to the effect of ptosis upon the gastric secretion, subacidity is the rule as shown in patients examined by the writer; as the dilatation became more marked the hydrochloric acid diminished, and was absent in most of the patients with very high grades of dilatation.

Nephroptosis.—This has absorbed by far the greatest amount of attention and study, an unfortunate condition in many ways, because to it have been ascribed many of the symptoms which undoubtedly are due to the displacement of other organs. Some, such as Israel, Litten, Morris, and Kuttner, believe that the so-called first degree of displacement of the kidney is not pathological. Harris, who is a firm believer in the congenital origin of nephroptosis, and who found a movable tenth rib in 61 of 110 cases, believes that the characteristic sign is a peculiar body form, a marked contraction of the lower end of the middle zone of the body, with a diminution of the capacity of this portion of the body cavity. Becker and Lenhoff divide the distance from the suprasternal notch to the upper edge of the symphysis pubis by the least circumference of the abdomen, for the sake of convenience multiplying this by 100;

the average index was 77, and they found that if it was above 77 the kidneys could usually be felt, while if below 75, as a rule they could not be felt. Albarran, Sheldon, and others, have noted numerous cases in the same family.

Among the *symptoms* may be mentioned a feeling of lack of support in the back and flank, frequent urination, associated with burning sensations, which is sometimes diagnosed and treated as cystitis, and pain which may be continuous or intermittent, and which is often relieved by the patient lying down. There may be intermittent hydronephrosis with polyuria after the reduction of the kidney to its normal position, and the so-called *Dietl's crises*, consisting of paroxysmal attacks of intense pain, nausea, and vomiting, according to some due to intermittent hydronephrosis, according to others to torsion of the renal vessels and nerves. Blood, albumin, and casts may occur in the urine. Some patients complain of feeling a moving mass in the abdomen, others have symptoms of sciatica and crural and intercostal neuralgia. Intermittent hematuria and nephritis have been described, while in some cases of post-operative pyelitis examined by the writer the fact that the affected kidney was in each case the displaced organ suggests that its resistance is lowered by the displacement.

Burnam finds that only 1 case in 10 of movable kidney has marked local symptoms, the cardinal symptoms being pain in the side, gastric symptoms, and nervousness. The dragging dull pain in the flank is about three times as common as acute attacks of Dietl's crises. About 1 out of every 8 cases with Dietl's crises shows a beginning hydronephrosis, about 1 out of every 3 cases shows marked gastric symptoms, and 1 out of every 3 cases shows pronounced nervous symptoms. Tuffier believes the gastric symptoms in nephroptosis are due to an atonic gastric dilatation, while of the paroxysmal pains in the renal region he describes two kinds: first, slight pain followed by the passage of much clear urine, and second, the pain associated with intermittent hydronephrosis, a renal tumor usually being made out during the paroxysm, while the amount of urine, which is markedly diminished with the onset of the pain, is often markedly increased with its subsidence, part of this increased flow being due to reflex stimulation of the healthy organ. Kelly, by catheterization of movable kidneys, has shown that a slight hydronephrosis is the rule, for he found the average capacity of the renal pelvis in 65 cases of nephroptosis to be between 12 and 13 cc., the normal capacity being 7 to 8 cc.

A causal relationship between nephroptosis and dilatation of the stomach is highly improbable. It seems likely that the dilatation of the stomach so frequent in splanchnoptosis is in the vast majority of cases etiologically dependent upon the gastroptosis. and that there is no usual causal relationship between it and floating kidney. Some have called attention to the relationship between floating kidney and obstruction of the common bile duct.

Hepatoptosis.—Floating liver is frequently not diagnosed, due partly to the difficulty in making out a moderate degree of displacement, partly because it is frequently regarded as an enlarged liver and partly because by the vast majority of observers the kidney is the only organ

carefully investigated in splanchnoptosis; yet the tables of Graham, Einhorn, Landau, and others show that the condition is not rare. The *symptoms* of the condition are rather indefinite. There may be spontaneous pain, which is sometimes brought on by jumping, walking, raising the right arm, sneezing, coughing, and yawning, while sometimes paroxysms of pain occur without apparent cause. In the writer's experience pain has been a very common symptom, usually relieved by making the patient lie on the back or on the right side, or by manual replacement of the organ. The pain is commonest in the right hypochondriac and epigastric regions, radiating thence toward the shoulder or the flank. Pressure, although rarely painful, often produces peculiar sensations in various portions of the body, especially the arms and shoulders.

Many patients complain of digestive symptoms, meteorism, constipation, or of feeling a movable body, colicky pains, respiratory disturbances, palpitation and jaundice. Keith believes that they are caused by the compression of the bile, blood, nerve, and lymph channels contained in the gastrohepatic omentum and that gall-stones are very commonly associated. Steele showed by experiments on a cadaver that biliary obstruction is met with in floating liver, pressure in the common duct being between two and three times the normal. Landau describes three grades of hepatoptosis: (1) moderate descent with anteversion or retroversion; (2) marked descent either with lateral displacement toward the right, or with anteversion or retroversion; (3) vertical or oblique displacement, the left lobe descending into the abdominal cavity.

Descent of the Intestines.—This is practically met with in every case of spanchnoptosis and the intestinal symptoms are many and diversified; among them may be mentioned constipation, fermentative dyspepsia, mucous colitis, which is quite common, various symptoms due to spasm or stenosis of the intestines, marked fulness in the lower half of the abdomen, and peristaltic movements in the displaced intestines, often made out if the abdominal wall is thin. Ewald believed that the intestinal disturbbances are due to the dragging of the bands on which the sections of intestines are hung, producing reflex irritation of the intestines, disturbances in their circulation, their motor and secretory functions, while, due to the sinking of the transverse colon, the horizontal portion of the duodenum is pulled downward. It is possible that a low grade of peritonitis may develop from the persistent fecal stasis, and that this may be the cause of Lane's band, Jackson's veil, etc. The small intestines, containing liquid feces, are but slightly affected by ptosis, but in the large intestines, containing solid feces, a loop or kink is of much more serious importance and may produce marked constipation, extreme stasis of the intestinal contents, and a train of symptoms which, by some, are regarded as neurogenic in origin, by others as due to a form of subinfection, and by others still as representing a true autotoxemia of intestinal origin. A kinked or a redundant sigmoid is often the cause of intractable constipation.

Descent of Spleen and Pancreas.—The descent of the *spleen* has been rarely described, because it is difficult to recognize slight displacements and because symptoms are usually absent. The patients complain of dragging, uneasy sensations in the back and side. All grades of splenic

displacement have been described, while the fact that several cases have been found in members of the same family suggests a congenital origin. The organ is usually enlarged, while sometimes torsion of the pedicle may occur with gangrene.

As regards the *pancreas*, a segment of this organ is firmly bound to the radix mesenterica, and is, therefore, fixed, but Ewald believed that the other portion may undergo descension, and may be felt as a constricted cord, which Glénard believed to be the transverse colon.

Diagnosis.—The diagnosis of splanchnoptosis should be easily made by all careful observers. It can often be made when the patient is first seen; the characteristic body form, the expression frequently described as juvenile and the evident psychasthenic tendency so frequently associated with splanchnoptosis call our attention to the possibility of this condition. Harris, Becker, Lenhoff, and others have expressed this peculiar body form mathematically, and the measurements are often very suggestive. Others insist on the importance of a floating tenth rib in this condition. In all cases the vague and protean symptom-complex of nervous and digestive disorders, inability to do hard mental or physical work, and the other symptoms described should make us suspect the condition. We must remember that many patients show no symptoms whatsoever, and in such the diagnosis can only be made by a careful physical examination.

As regards the diagnosis of *gastroptosis*, splashing or succussion sounds are frequently heard, there is commonly a sinking in of the epigastrium, with a bulging in the region of the umbilicus or below it, while if the abdominal wall is thin peristaltic waves may occasionally be definitely seen. The position of the stomach may be determined by distending it with gas, but the roentgen-ray examination gives us so much more exact data that it has practically supplanted other methods. The stomach should be examined in upright and prone positions, and the size and position of the cap and the emptying time noted. The fish-hook, vertical, cowhorn (crescent, half moon), and spasmodic hour-glass forms have been described. From roentgen-ray examinations the position of the normal stomach and intestines is lower than that described by the anatomists, this in part being due to the fact that most fluoroscopic examinations of the gastro-intestinal tract are made in the upright position.

In *nephroptosis* sometimes the displaced kidney can be distinctly seen through the thin abdominal wall, while in many cases a sinking in of the flanks can be noted. The only satisfactory method is by bimanual palpation of the organ. The patient should be examined both in the standing position, lying on the back, and lying on either side, while it is extremely important in many cases to make the patient walk around, hop, jump, or support herself with both hands on the side of the bed before making the examination. If the abdominal walls are rigid, palpation in a hot bath is helpful. Many mistakes have been made by examining patients in bed after a night's rest when the kidney has returned to its normal position. Lifting up the kidney with the fingers and its palpation with the thumb is a simple and easy method of determining

displacement of this organ. In *Dietl's crises* a tumor in the lumbar region is frequently made out, which disappears on the cessation of pain. It is unquestionable that too frequent or too severe palpation of the kidneys may harm these organs, and albumin, casts, and blood may be found after such an examination.

In *hepatoptosis* we practically always find a tumor in the right side of the abdomen with its convex surface directed forward. In making the diagnosis we use both palpation and percussion. On percussion the liver dulness, instead of beginning at the fifth rib or fourth or fifth interspace in the mammillary line, is at a much lower level, often the costal margin, while the lower limit of dulness is correspondingly depressed. When the patient lies on his back or his right side with the hips elevated, the liver sometimes falls back into its normal position, and the topographical percussion is normal. For this reason it is important to percuss first with the patient in the erect position. By bimanual palpation we can make out the characteristic tumor in the hypochondriac or lumbar region; the patient must be examined in both the prone and upright position, and an attempt made to replace the organ. Because of its rotation the liver always seems enlarged. Sometimes by inpection a slight bulging of the abdomen on the right side is made out. We must remember that sometimes replacement is impossible because of adhesions, while in all cases we must differentiate a displacement which is part of a general splanchnoptosis from that due to pleurisy with effusion, diaphragmatic abscess, or from enlargement or tumors of the liver.

In diagnosing displacement of the *intestines*, the only really satisfactory method is the use of the roentgen-rays, bismuth or barium being given by mouth or by enema. By palpation, the cecum is often felt distended, and the descending colon and sigmoid contracted as thin cords. By distention through a rectal tube by air we can usually determine satisfactorily the position of the transverse colon. The pulsation of the abdominal aorta can usually be easily felt. The low position of the hepatic and the high position of the splenic flexure, and the fact that the contents appear to remain longer in the cecum than elsewhere have been specially noted in roentgen-ray examinations.

The diagnosis of *splenoptosis* is usually easy, as by palpation the organ with its sharp edge and notch may be easily made out. If, however, the organ is fixed in an abnormal position and deformed by adhesions the diagnosis is much more difficult.

As a rule, the diagnosis of splanchnoptosis should be easily made. In women from a careless examination the condition is frequently regarded as a purely gynecological one, while in some cases gastroptosis with the cachexia sometimes associated with it has been mistaken for gastric ulcer or carcinoma. Among the conditions which may be mistaken for floating kidney are fecal tumors in the hepatic flexure or in a loop of the small intestine, a distended gall-bladder, a myoma of the uterus with a long, thin pedicle, or a small ovarian cyst or tumor. Among the conditions for which floating liver has been mistaken may be mentioned renal tumors and hydronephrosis, nephroptosis, and certain rare cases of thickened mesentery or omentum. The spleen has occasionally been mistaken for a uterine myoma, or an ovarian cyst or tumor.

Prognosis.—In many patients no symptoms are present and no treatment is necessary. If they are seen early and are willing and able to carry out prophylactic measures, or in those cases in which the symptoms are almost exclusively referable to one displaced organ, real success may attend the treatment, be it medical or surgical; but in the majority of cases in adult life, when the organs show considerable displacement, the symptoms are marked and varied and the nervous system considerably involved, although the condition may be relieved in many cases and in some the symptoms made to entirely disappear, yet there will be a large number in whom treatment is discouraging.

Treatment.—The treatment is in the main rather unsatisfactory, particularly so if the symptoms have been present a long time and the displacement of the various viscera has reached a marked degree. In the majority of cases the condition in all probability depends on a congenital fragility of tissue, while in those so disposed numerous secondary factors have brought about the displacement of the various viscera.

Prophylaxis.—To prevent marked manifestations of splanchnoptosis it is most important that the tendency should be recognized early and every possible method of prophylaxis carried out. Children with the characteristic body form, or with a slight displacement of any of the abdominal viscera, should be treated with the utmost care; they should be made to lie down during certain hours of the day, especially after meals; great care should be paid to their diet, and if they are extremely thin every effort made to fatten them; the strength of the diaphragm, the intercostals, and the abdominal muscles should be increased by carefully chosen exercises; they should be given breathing exercises, in hope of enlarging the lower thoracic zone; sometimes they should be made to wear abdominal bandages for a short period of time if their abdominal muscles show great lack of tone; abdominal massage should be given if possible, and everything should be done to put them and to keep them in the best possible physical condition.

Attention should be paid to all persons, whether adults or children, during and after acute or chronic diseases associated with marked loss of weight or diminution of muscular tone, and one should be most careful about allowing such patients to get up from bed and go back to active occupations. Systematic overfeeding with massage should be carried out to bring body weight and muscle tone to normal. Great care should be taken after rapid obesity cures, and it is probable that in this, as well as in a number of the other above conditions, wearing a bandage for a short period is advisable. Too much care cannot be taken during the puerperium. The patient should not be allowed to get up too soon, and when she does she should be provided with a snug abdominal support until the mechanical conditions within the abdomen approximate normal. Great care and practically the same precautions should be taken after the removal of large quantities of ascitic fluid or of large abdominal tumors, for in these conditions, as in pregnancy, there is a sudden diminution of intra-abdominal pressure. It is essential that physicians should demonstrate to their patients the dangers from the use of tight corsets or tight belts, and if they insist upon their continuance try to persuade

them to wear the less unhealthful kind, that is, the straight front corset, in which the pressure is exerted upon the lower half of the abdomen. The great majority of patients with splanchnoptosis are deficient in body fat, and even when no symptoms are present we should advise such patients to so regulate their diet and mode of life that an increase in weight will take place. Patients with this tendency should systematically carry out breathing and other exercises to improve the tone of their respiratory and abdominal muscles.

General Treatment.—The diet in splanchnoptosis depends largely upon the degree to which the stomach and intestines are involved. Ample nutrition to increase the body weight is most important, and this is best obtained by following a simple mixed dietary with little fluids at meals, while often between meals raw eggs and milk are given; in some cases intermediate feedings are not well borne, in other cases the patient may be put at first on an absolute milk diet associated with rest. By these methods weight can be added with practically always a marked improvement; we must be extremely careful not to overload the stomach and not to increase the tendency toward dilatation. Often it is advisable to insist that the patient lie down for some time after each meal.

We should advise our patients against wearing tight clothing, and especially against wearing anything that constricts the lower half of the thorax. Great benefit can be derived from carefully selected outdoor exercises and Swedish movements, although these must not be overdone; in fact, it is wise to begin very gently and to gradually increase as the tone of the abdominal muscles improves. Patients should be taught the proper mode of breathing and of standing. Both abdominal and general massage is of real value in this condition. Good results are obtainable with "cannon-ball" massage, which the patient can give himself.

It has been frequently observed that after rest in bed, especially with the foot of the bed elevated, these patients often show marked improvement, especially in cases of marked gastroptosis with some dilatation, and a strict rest cure often produces splendid results. In some cases during pregnancy the symptoms are markedly relieved.

Hydrotherapy is often helpful both as regards the gastro-intestinal and the nervous symptoms, and the Scotch douche has been found specially beneficial. In cases of associated dilatation of the stomach lavage is occasionally indicated in association with a careful diet.

Medicinal Treatment.—Medicine plays but a very small part in the treatment. For constipation we should first try massage, and exercise, diet, and hydrotherapy; if these do not prove effectual, enemata may be given, especially those of oil, while if laxatives are necessary, we may use mineral oil, agar, bran, psyllium seeds, or, if these are not effective, any simple laxative such as senna, cascara, phenolphthalein, etc. Sometimes a morning saline is effective. If anemia is present, iron and arsenic are indicated, although each must be used with care, because they may increase the gastro-intestinal symptoms. Hypodermics of cacodylate of soda or of iron are very useful. As a general tonic nothing is so good as strychnine in increasing doses. As regards water, but little should be taken with the meals, as a rule, but a considerable amount should be

taken on waking, in the middle of the morning and afternoon, and at bedtime; the alkaline waters are especially satisfactory. We may give alkalis for hyperchlorhydria, hydrochloric acid and bitter stomachics for subacidity and anacidity.

Mechanical Supports.—The use of various mechanical supports in association with the measures already described has proved of great value. The object of the support is to lessen the volume of the lower half of the abdomen and to increase intra-abdominal pressure; to get satisfactory results it is essential that the corset or belt should be applied with the patient in the inclined dorsal position, so that the various viscera are in their positions of least descension. The support is dangerous if it is not well made or applied improperly, because if the pressure is above any of the displaced viscera it increases the descension, and unless the patient carries out systematic abdominal exercises the use of the bandage is likely to decrease the tone of the abdominal muscles. As a rule, when its use is associated with the proper dietetic, hygienic, and medicinal measures, a disappearance of many of the symptoms results in the majority of cases.

Many different kinds of bandages have been recommended: Glénard advises an elastic bandage with straps; Rose one made of adhesive plaster; Gallant a corset made to fit the patient and laced from below upward with the patient in the inclined dorsal position. Ewald and Kuttner use besides the bandage a pad in kidney displacements, Riegel a pad or bolster in gastroptosis, Enriguez a pneumatic pad.

Operative Treatment.—It formerly was a moot question whether splanchnoptosis is a medical or a surgical condition. It seems now that in the vast majority of cases it is strictly medical, and only surgical when the symptoms are so definitely referable to one organ that suspension will offer a good chance of the disappearance of the symptoms; in *every* case hygienic, dietetic, and mechanical measures should be faithfully tried first. Among the indications for surgical interference may be mentioned those cases in which practically all the symptoms are referable to the displacement of one organ. In the case of the *kidney,* Dietl's crises, intermittent hydronephrosis, symptoms suggestive of renal or hepatic colic, more or less constant pain, symptoms due to pressure of the displaced kidney upon other organs, or upon the sympathetic or genitocrural nerves, are all indications for operative treatment; and also, as Kelly has shown, when the attacks of pain may be reproduced by injecting salt solution into the renal pelvis through a ureteral catheter. In the case of the *liver,* pain of a tearing, twisting character if frequent, attacks like hepatic colic, and symptoms due to pressure on other organs, in the case of the *spleen,* torsion of the pedicle with swelling and gangrene, in the case of the *intestines,* constipation which does not yield to *any* medicinal or mechanical treatment, are indications for surgical measures. It seems also justifiable to try operative measures in those patients with marked symptoms when all other methods have failed.

In operating upon the *stomach* various methods have been devised. Duret, in 1896, stitched the stomach to the abdominal wall; Lambotte attached by suture the splenic and hepatic flexures to the abdominal wall, thus lifting up the stomach; Webster resected the abdominal wall,

bringing together the recti, which had undergone diastasis; Walker performed gastrojejunostomy; Eve operated by placing sutures through the lesser curvature, the lesser omentum, and the liver substance; Coffey by suspending the stomach in a hammock made by the great omentum; Blecher and Bier by shortening and folding the gastrohepatic ligament. Beyea passed sutures through the gastrohepatic and gastrophrenic ligaments, the stomach by this method not being fixed, but elevated into its normal position without affecting its mobility; while in cases of gastroptosis with marked dilatation, gastro-enterostomy or perhaps in some cases pyloroplasty, may be performed. It must not be forgotten that in some of these cases fixation is followed by dilatation, persistent vomiting, and even by marked thinning of the stomach wall and in our experience *none* of the above operations is usually justifiable. If the drag of the ptosed atonic organ, for a long period of time upon the pyloric-duodenal region has produced a partial obstruction, a Finney pyloroplasty may prove very beneficial.

As regards fixation of the *kidney*, many methods have been described, such as suture through the fatty capsule alone, through the fibrous capsule alone, through the kidney substance, splitting and dissecting the capsule and stitching it to the lumbar muscles, and packing with gauze, which is kept in until firm adhesions form. Most operators advocate suture of the parenchyma in addition to a free dissection of the fibrous and fatty capsule, while Kelly insists upon the Brödel stitch. Wehrmann and Harris believe that the tendency has been to stitch the kidney too high, as the liver may again press upon the upper pole and bring about a recurrence. Relapses after nephropexy are due to this or to insufficient fibrous union between the kidney and the lumbar muscles; in some cases the kidney is fixed in the wrong position and the function of ureter and bloodvessels markedly interfered with; in women a satisfactory nephropexy is peculiar difficult because of the greater obliquity of the lower ribs. Certainly at present nephropexy seems justifiable only in intractable cases of Dietl's crises which do not yield to postural, supporting, upbuilding treatment.

The mortality in nephropexy is practically *nil*. Burnam found that 90 per cent. were cured of pain, about the same number showed a relief of stomach symptoms, while 50 per cent. were improved nervously; the results when both kidneys were movable were practically the same as in the case of unilateral disease if both were suspended. Tuffier found that the results of fixation of displaced kidneys when hydronephrosis is present are not so good as in cases in which it is absent, for while the operation relieves the pain, the prolonged distention has affected the organ so that it never regains its normal tone. Treves, from a study of 300 cases held that suturing of the kidney should be a rare operation, for as good, if not better, results are obtained by the use of mechanical supports.

As regards fixation of the *liver*, hepatopexy, various operations have been performed. Billroth and others sutured the liver to the abdominal wall, Langenbech selected the lower costal cartilages as the points of fixation, some produced adhesions between the convexity of the liver and

the diaphragm by irritation of their surfaces, while others sutured the fundus of the gall-bladder to the parietal peritoneum. Rovsing reported 18 hepatopexies with good results. In most cases movable *spleen* requires no special treatment, but with torsion of the pedicle and symptoms of stasis or pressure upon other organs, splenectomy has been done.

In displacement of the *intestines* considerable surgical work has been done. In the case of the small intestines, filled with liquid feces, ptosis produces comparatively slight symptoms, but the presence of solid feces in the large intestines means that descension is frequently associated with persistent and intractable constipation, this being especially so in ptosis and kinking of the sigmoid. To counteract this, various operations have been performed, suspension of the sigmoid flexure (sigmoidopexy) and even resection of the sigmoid. Resection of the colon as formerly practised by Lane has been practically given up, although an occasional right sided partial colectomy has been done with success where atony and stasis, of maximum degree, were practically localized in this section of the gut. Appendicostomy and cecostomy or colostomy, with subsequent lavage of the intestine for a long period through the new opening, have been done in the hope of relieving the symptoms in certain cases of very marked enteroptosis, especially those in which many adhesions are present or when constipation is intractable.

INDEX.

A

Abdomen in acute enteritis, 540
peritonitis, 918
in ascites, 901
in carcinoma of stomach, 417
in cholera nostras, 541
in chronic enteritis, 544
perihepatitis, 785
peritonitis, 958
in cirrhosis of liver, 814
of stomach, 482
in mesenteric embolism, 643
thrombosis, 643
in mucous colitis, 645
in nervous dyspepsia, 368
in splanchnoptosis, 992
in subphrenic pyopneumothorax, 949
in tuberculosis of peritoneum, 963
Abdominal distention in appendicitis, 579
muscles, constipation and, 525
operations, acute dilatation of stomach and, 451
organs, anatomy of, 986
embryology of, 986
viscera, correlation of, through vagus and sympathetic, 241
wall, perforation of, in gastric ulcer, 393
Abscess in appendicitis, 578
in diabetes mellitus, 146
hepatopulmonary, 796
of liver, 790
diagnosis of, from carcinoma, 837
of mesentery, 934
of omentum, 935
of pancreas in calculus of pancreas, 695
periappendicular, 572
pericolic, 936
perigastric, 935
residual, peritoneal, 937
retroperitoneal, 937
rupture of, acute peritonitis and, 911
of spleen, subphrenic abscess and, 939
subphrenic, 937
Absorption of foods in intestine, 500
Acetic acid in carcinoma of stomach, 420
Aceto-acetic acid, 50
Acetone in diabetes mellitus, 144
Acholic stools, 503
Achroöcytosis, 281
Achylia gastrica, 236, 357
course of, 360
in chronic gastritis, 451
Achylia gastrica, diagnosis of, 360
from chronic gastritis, 453
diarrhœa in, 359
etiology of, 357
gastric contents in, 359
neurasthenia and, 358
pain in, 359
pathology of, 358
prognosis of, 360
symptoms of, 359
treatment of, 360
vomiting in, 359
Acid foods, 71
Acid-base equilibrium, 72
Acidity, gastric, in duodenal ulcer, 406, 556
in gastric ulcer, 385
Acidosis, 72
in cholera infantum, 551
in diabetes mellitus, treatment of, 165
Acids, metabolism of, 70
Acne of mouth, 262
pancreatica, 701
Acoria, 361
diagnosis of, 361
etiology of, 361
from bulimia, 333
symptoms of, 361
treatment of, 361
Acromegaly, diabetes mellitus and, 120
glycosuria and, 120
metabolism in, 128
Actinomyces bovis in mouth, 266
Actinomycosis of appendix, 593
of cheek, 266
of jaw, 266
of lips, 266
of mouth, 266
of œsophagus, 289
Acute yellow atrophy of liver, 767
Addison's disease, diagnosis of, from acute peritonitis, 927
Adenitis in carcinoma of stomach, 417
Adenoma of intestines, 639
endometrial, 640
of pancreas, 410
Adenomatous carcinoma of stomach, 412
Adhesions, abdominal, digestion and, 242
in chronic peritonitis, 957
of gall-bladder, 877
of intestines, carcinoma and, 633
peritoneal, gastric, 391
intestinal obstruction from, 613
Adiposis dolorosa, 216
diagnosis of, from obesity, 216

Adiposity, 209
exogenous, 210
gonad, 215
pituitary, 215
Adrenal glands, carbohydrate metabolism and, 127
diabetes mellitus and, 127
Aërophagia, 341. *See* Nervous eructation.
Aglossia, 268
Agusia, 251
Albuminuria in appendicitis, 579
in ascites, 902
in cirrhosis of liver, 810
in diabetes mellitus, 145
in gout, 197
in nephroptosis, 995
Albumoses in carcinoma of stomach, 417
Alcohol, metabolism of, 64
obesity and, 211
Alcoholic neuritis in cirrhosis of liver, 818
Alcoholism, acute hepatitis and, 788
yellow atrophy of liver and, 768
carcinoma of stomach and, 410
chronic gastritis and, 446
interstitial pancreatitis and, 688
peritonitis and, 955
cirrhosis of liver and, 801, 826
fatty liver and, 762, 763
tuberculosis of peritoneum and, 960
Aldoses, 42
Alimentary disorders in gout, 196
glycosuria, 133
Alkalies, metabolism of, 70
Alkaline reserve in diabetes mellitus, 152
Alkapton, 143
Alloxuric bodies in diabetes mellitus, 145
in gout, 181
Amino-acids, 52
Aminolipins, 48
Ammonia nitrogen, 64
in urine in diabetes mellitus, 144
Amœba in carcinoma of stomach, 422
Ampulla of Vater, carcinoma of, 888
diagnosis of, 893
pathology of, 890
symptoms of, 892
treatment of, 893
Amyloid degeneration, intestinal hemorrhage and, 517
of liver, 763
disease of intestines, 599
diagnosis of, from tuberculosis, 596
liver, ascites and, 897
diagnosis of, from fatty liver, 763
Amylopsin, 499
Amyxorrhœa gastrica, 332
Anacidity, gastric, 357. *See* Achylia gastrica.
Anemia in amyloid liver, 764
in carcinoma of intestines, 637
of stomach, 417
gastric ulcer and, 375
intestinal hemorrhage and, 517
pernicious, diagnosis of, from sprue, 654
Anemia, pernicious, mouth in, 263
pigmentation of liver and, 765
splenic, diagnosis of, from cirrhosis of liver, 819
in sprue, 649, 654
Anemic obesity, 213
Anesthesia of mouth, 250
Aneurism of aorta, diagnosis of, from cyst of pancreas, 707
of hepatic artery, 754
miliary, hematemesis and, 488
ruptured, diagnosis of, from necrosis of pancreas, 680
Angina, Ludwig's, 282
Angioma of lips, 253
of liver, 838
of peritoneum, 972
of tongue, 268
Angioneurotic œdema, diagnosis of, from appendicitis, 588
of œsophagus, 289
Angiosclerotic dyspragia of intestines, 644
Anomalies of biliary ducts, 839
of gall-bladder, 839
of liver, 751
of tongue, 268
Anorexia in carcinoma of stomach, 415
in chronic gastritis, 450
nervous, 362
appetite in , 362
constipation in, 362
diagnosis of, 362
etiology of, 362
inanition in, 362
symptoms of, 362
treatment of, 362
in syphilis of stomach, 493
Anthracosis, hepatic, 764
Antibodies, gastric ulcer and, 376
Antiketogenic factors in diabetes mellitus, 157
Antiperistalsis of intestines, 496
pathological, 497
Antiseptics, intestinal, 508
Aorta, aneurism of, diagnosis of, from cyst of pancreas, 707
ruptured, diagnosis of, from necrosis of pancreas, 680
Aphthæ, Bednar's, 259
Aphthous stomatitis, 254
Apoplexy, pancreatic, 669
Appendicitis, 564
abdominal distention in, 579
abscess in, 572, 578
of liver and, 791
albuminuria in, 579
ascaris lumbricoides in, 568
bacteriology of, 569
catarrhal, 570, 580
chills in, 577
cholelithiasis and, 865
chronic, 573, 583
peritonitis and, 952
relapsing, 582
treatment of, 592
constipation in, 576
contents of appendix in, 571

Appendicitis, cystitis in, 579
definition of, 564
diagnosis of, 583
character and stage of, 584
from acute cholecystitis, 860
colitis, 585
enteritis, 585
gastritis, 585
pancreatitis, 586
peritonitis, 588
pyelitis, 587
from angioneurotic œdema, 588
from biliary colic, 587
from cholecystitis, 587
from cholelithiasis, 587
from cholera nostras, 542
from duodenal ulcer, 558
from gastric ulcer, 391
from Henoch's purpura, 588
from hysteria, 588
from intestinal colic, 515, 585
obstruction, 586
from malarial fever, 586
from movable kidney, 588
from nephrolithiasis, 587
from nervous conditions, 588
from oöphoritis, 588
from ovarian neuralgia, 588
from pancreatitis, 586
from pneumonia, 586
from renal colic, 587
from rupture of duodenal ulcer, 558, 586
of gastric ulcer, 586
from salpingitis, 588
from typhoid fever, 586
diarrhœa in, 576
digestive disturbances in, 567
etiology of, 567
fecal concretions in, 568
fever in, 576
foreign bodies in, 568
gangrene in, 571
gangrenous, 580
heredity in, 567
hyperacidity in, 317
hyperalgesia in, 575
involvement of whole appendix in, 581
leukocytosis in, 577
lymphoid tissue and, 569
McBurney's point in, 575
mild, 581
nationality in, 567
nausea in, 576
occupation in, 567
oxyuris vermicularis in, 568
pain in, 574
parasites and, 568
pathology of, 569
peritonitis in, 572, 579
prognosis of, 589
diffuse peritonitis and, 590
perityphlitis and, 589
pulse in, 577
relapsing, 582
rigidity in, 575
septicemia in, 580
Appendicitis, sex in, 567
signs of, 578
simple, 580
sulphrenic abscess and, 938
surrounding structures in, 572, 581
symptoms of, 574
infectious, 576
reflex, 576
vesical, 579
treatment of, 590
diet in, 591
medical, 591
trichuris trichiura in, 568
tumor in, 578
urine in, 579
varieties of, 580
vomiting in, 576
Appendicular abscess, subphrenic pyopneumothorax and, 949
colic, 581
Appendix, actinomycosis of, 593
anatomy of, 565
carcinoma of, 593
circulation of, 566
coats of, 566
contents of, 571
cystic distention of, 593
diseases of, acute peritonitis and, 911
gangrene of, 571
inflammation of, 564. *See* Appendicitis.
lymphatics of, 566
mucocele of, 593
myoma of, 593
myxoma of, 593
necrosis of, 571
nerve supply of, 567
obliteration of, 573
polyps of, 593
sarcoma of, 594
secondary, 594
tuberculosis of, 592
tumors of, 593
prognosis of, 594
Appetite in atony of stomach, 365
in constipation, 525
in diabetes insipidus, 175
mellitus, 140
in hyperacidity, 318
in nervous anorexia, 362
dyspepsia, 368
in obesity, 214
perversion of, 334, 362
Aptyalism, 276
Arterial mesenteric thrombosis, 641
Arteries in diabetes mellitus, 148
Arteriosclerosis, chronic peritonitis and, 688, 955
diabetes mellitus and, 664
in gout, 193, 197
of intestines, 643
peritonitis and, 955
Arthracotic cirrhosis of liver, 822
Arthritis deformans, diagnosis of, from gout, 200
in gout, 191, 194
Ascaris, appendicitis and, 568

Ascaris, hemorrhagic pancreatitis and, 672
in necrosis of pancreas, 672
Ascites, 896
abdomen in, 901
in acute perihepatitis, 781
albuminuria in, 902
amyloid liver and, 897
backward pressure and, 896
bacteriology of, 899
in carcinoma of gall-bladder, 891
of liver, 834
of pancreas, 712
cells in 899, 904
in chronic perihepatitis, 786
peritonitis, 958
chyliform, 900
chylous, 899
cirrhosis of liver and, 815, 897
of stomach and, 482
in congestion of liver, 778
constipation in, 902
in cyst of pancreas, 705
diagnosis of, 903
as to cause, 904
from intestinal obstruction, 903
from ovarian cyst, 903
dyspepsia in, 902
etiology of, 896
exudates in, 898
fatty, 900
lactescent, 900
milky, 900
non-fatty, 900
palpation in, 902
pathology of, 898
percussion in, 902
peritonitis and, 897
prognosis of, 905
renal dropsy and, 898
results of, 902
signs of, 901
syphilis of liver and, 897
in thrombosis of portal vein, 759, 898
transudates in, 898
treatment of, 905
diuretics, 907
operative, 907
paracentesis in, 906
purgation in, 907
in tuberculosis of peritoneum, 963
Ascitic fluid, character of, 898
tuberculosis of peritoneum, 963
Asthma in gout, 197
non-surgical drainage of biliary tract, in, 749
Atonic constipation, 523
Atony, gastro-intestinal, hyperacidity and, 319
of stomach, 364. *See* Stomach, atony of.
diagnosis of, from hyperacidity, 320
Atophan in gout, 206
Atrophy of liver, 760
acute yellow, 767
of mucous membrane, diagnosis of, from carcinoma of stomach, 425
Atrophy of salivary gland, 282
of tongue, 274
Atwater-Rosa-Benedict respiration calorimeter, 24
Auto-intoxication, constipation and, 526
Auto-inoculation in carcinoma of stomach, 416
Automatic mechanism in intestinal processes, 501
Avellis, syndrome of, paralysis of œsophagus and, 290
Azotorrhœa in calculus of pancreas, 696
in disease of pancreas, 660

B

Bacillus acidophilus in intestines, 505
aërogenes capsulatus in acute peritonitis, 913
in appendicitis, 569
gaseous liver and, 761
in infections of biliary tract, 842
in intestine, 505
in necrosis of pancreas, 670
in suppurative cholangitis, 849
bifidus communis in intestines, 505
Boas-Oppler in carcinoma of stomach, 421
bulgaricus in intestines, 509
coli in acute peritonitis, 912
yellow atrophy of liver and, 768
in appendicitis, 569
in chronic peritonitis, 956
in diarrhœa, 534
in childhood, 548
in fat necrosis of pancreas, 665
in infections of biliary tract, 842
in intestines, 505
in necrosis of pancreas, 670
in suppurative cholangitis, 849
dysenteriæ, diarrhœa and, 534
enteritidis in diarrhœa, 535
gingivitidis in mouth, 263
lactis aërogenes in appendicitis, 569
in diarrhœa in childhood, 548
in infections of biliary tract, 842
in intestines, 505
in necrosis of pancreas, 670
putrificus in intestines, 505
pyocyaneus in acute peritonitis, 912
in appendicitis, 569
in diarrhœa, 535
in infections of biliary tract, 842
in suppurative cholangitis, 849
subtilis in infections of biliary tract, 842
tuberculosis in chronic peritonitis, 956
typhosus in infections of biliary tract, 842
in peritonitis, 913, 956
in suppurative cholangitis, 849
Backache in gastric ulcer, 381

Bacteria in abscess of liver, 790
in acute enteritis, 539
in constipation, 521
in intestines, distribution of, 505
necrosis of pancreas and, 670
Bactericidal function of liver, 724
Bacteriology of acute cholecystitis, 854
peritonitis, 912
of appendicitis, 569
of ascites, 899
of biliary infections, 842
of cholelithiasis, 854
of diarrhœa, 534
of gangrenous stomatitis, 257
of intestinal tract, 504
of mouth, 245
of subphrenic abscess, 945
of suppurative cholangitis, 849
pancreatitis, 682
of tuberculosis of peritoneum, 960
of ulcerative stomatitis, 255
Bacteriophage, 507
Bacteriophagum intestinale, 507
Baelz's disease, 253
Banti's disease, diagnosis of, from cirrhosis of liver, 819
Basal metabolism, 28
in fasting, 35
Benedict's studies on students, 37
chronic inanition in, 36
in health, 73
standards of, 74, 79
surface area in, 75, 78
tests, management of, 28
Bednar's aphthæ, 259
Belching, 341
Benedict cot-chamber, 26
portable respiration apparatus, 26
student respiration apparatus, 27
universal respiration apparatus, 26
Bernheim's liver functional tests, 728
Bile, 499
amount of, 718
changes in, 730
components of, 718
duct, common, obstruction of, 875
biliary tract infection through, 842
non-surgical drainage of, 742
fractions of, 745
hemorrhagic pancreatitis and, 671
Kupffer cells and, 736
pigments, formation of, 717
salts, formation of, 717
secreting function of liver, 716
thrombi, 735
white, 741
Bilharzia hæmatobia, portal cirrhosis and, 802
Biliary calculi, diagnosis of, from calculi of pancreas, 697
cirrhosis of liver, 826
diagnosis of, from acute yellow atrophy of liver, 772
from carcinoma of liver, 836
Biliary cirrhosis, diagnosis of, from portal cirrhosis, 818, 830
colic, diagnosis of, from appendicitis, 587
from necrosis of pancreas, 679
ducts, abscess of liver and, 791
anomalies of, 839
carcinoma of, 886
diagnosis of, 892
etiology of, 887
pathology of, 889
primary, 887
prognosis of, 873
treatment of, 893
common, obstruction of, 875
congenital obliteration of, 839
diagnosis of, 840
symptoms of, 840
treatment of, 840
extrahepatic, carcinoma of, 887
fistulæ in cholelithiasis, 878
non-surgical drainage of biliary tract in, 749
intermittent fever, diagnosis of, from abscess of liver, 798
tract, cholelithiasis and, 864
digestion and, 240
infections of, 840
bacteriology of, 842
in cholelithiasis, treatment of, 882
through common bile duct, 842
lymphatic circulation, 844
portal circulation, 843
systemic circulation, 843
wall of gall-bladder, 844
vicious circles in disease of, 744
non-perforation of, peritonitis and, 925
non-surgical drainage of, 742
in asthma, 749
in biliary fistulæ, 749
in catarrhal jaundice, 749
continuous, 747
development of, 745
intermittent, 747
limitations of, 747
in obstructive jaundice, 748
in quiescent cholelithiasis, 748
in relapsing cholangitis, 748
results obtained in, 750
selection of cases for, 748
therapeutics of, 743
value of, in diagnosis, 745
as therapeutic procedure, 747
Bilirubin, formation of, 717

Bilirubin in liver, 765
renal threshold for, 727
van den Bergh test for, 726
Biliverdin in liver, 765
Black tongue, 269
Bladder, diseases of, acute peritonitis and, 911
rupture of periappendicular abscess into, 572
Bleeding, extragastric, 485
gastric, 484
Blood in abscess of liver, 796
in acute peritonitis, 922
yellow atrophy of liver, 771
in carcinoma of intestines, 637
of stomach, 414
in cirrhosis of liver, 817, 829
cultures in acute peritonitis, 922
in diabetes mellitus, 137
glucose in, forms of, 132
in gout, 190
in jaundice, 739
metabolism of, 65
in obesity, 213
"occult," tests for, 384, 385
in sprue, 654
sugar, 46
content in diagnosis of carcinoma of stomach, 423
in diabetes mellitus, 133
metabolism of, 46
renal threshold of, 133
supply, digestion and, 238
transfusion in sprue, 656
in tuberculosis of peritoneum, 964
uric acid in, 184, 185
Bloodvessels, diseases of, intestinal hemorrhage and, 517
in jaundice, 740
in portal cirrhosis of liver, 805
Boas-Oppler bacillus in carcinoma of stomach, 426
Body temperature, basal metabolism and, 93
Boils in diabetes mellitus, 146
Bowel, compression of, obstruction from, 614
congestion of, constipation and, 522
incarceration of, intestinal obstruction from, 613
infarction of, intestinal hemorrhage and, 517
inflammation of, intestinal hemorrhage and, 518
strangulation of, intestinal hemorrhage and, 517
ulceration of, 553
intestinal hemorrhage and, 518
β-oxybutyric acid in diabetes mellitus, 144
Bradycardia in jaundice, 740
Brain, lesions of, diabetes mellitus and, 121
tumors of, diabetes mellitus and, 121
Breath, odors of, 248, 250
offensive, 248
in abscess of lung, 250
in atony of stomach, 250
in carcinoma of larynx, 250
Breath, offensive, in chlorosis, 250
in cirrhosis of liver, 250
in diabetes, 250
in dilatation of stomach, 250
in diverticulum of œsophagus, 250
in gangrene of lung, 250
in hemoptysis, 250
in septicemia, 250
treatment of, 250
in tuberculosis, 250
in uremia, 250
Bronze diabetes, 123, 820
Budd's non-alcoholic cirrhosis of liver, 802
Bulimia, 333
in diabetes mellitus, 140
Burns, duodenal ulcer and, 558
Butyric acid in carcinoma of stomach, 420

C

Cachectic splanchnoptosis, 993
Cachexia in carcinoma of pancreas, 713
Calcium, metabolism of, 69
in sprue, 651
Calculus of pancreas, 693
diabetes mellitus and, 122
salivary, 279
tartar, 279
Calorimeter, 24
Cancer of stomach, 409. *See* Stomach, carcinoma of.
Cancrum oris, 256
Carbohydrates, absorption of, in intestines, 500
diabetes mellitus and, 119
diet, diabetes mellitus and, 119
digestion of, 45
formation of glucose from, 131, 157
metabolism of, 42
adrenals in, 127
in diabetes mellitus, 130, 131, 135
epinephrine and, 127
liver and, 720
hypophysis in, 128
normal, 131
parathyroids and, 129
in sympathicotonia, 127
thyroid and, 129
in vagotonia, 127
Carbohydrate-free diet in diabetes mellitus, 158
Carbuncle in diabetes mellitus, 146
Carcinoma of ampulla of Vater, 888
of appendix, 593
of biliary ducts, 886
of choledochopancreatic duct, 888
of colon, 635
of duodenum, 634
diagnosis of, from carcinoma of stomach, 426
of gall-bladder, 886
diagnosis of, from cholelithiasis, 880
of ileum, 635
of intestines, 631

Carcinoma of jejunum, 635
of lips, 253
of liver, 833
diagnosis of, from carcinoma of gall-bladder, 892
of stomach, 427
of mouth, 260
of œsophagus, 300
diagnosis of, from cardiospasm, 350
from hematemesis, 487
of pancreas, 709
diabetes mellitus and, 122
solidum, 707
of stomach, 409
diagnosis of, from achylia gastrica, 360
from chronic gastritis, 425
from cirrhosis of liver, 819
from diseases of pancreas, 427
from gastralgia, 336
from gastric ulcer, 390
from hypertrophic stenosis of pylorus, 428
from nervous dyspepsia, 369
gastralgia, 336
from perigastritis, 426
from spasm of pylorus, 428
from tumors of colon, 427
of gall-bladder, 427
of omentum, 427
from ulcers of pylorus, 428
hematemesis from, 488
of tongue, 274
Cardia, nervous control of, 308
spasm of, 347
Cardiac cirrhosis, 777
stenosis, gastric ulcer and, 395
Cardioptosis, incidence of, 991
Cardiospasm, 291, 347
acute dilatation and, 460
diagnosis of, 349
dilatation of œsophagus and, 347
dysphagia in, 349
etiology of, 347
hysteria and, 348
neurasthenia and, 348
pain in, 349
prognosis of, 350
symptoms of, 348
treatment of, 350
Cardiovascular lesions in gout, 193
system in diabetes mellitus, 138
Casts in diabetes mellitus, 145
Cataract in diabetes mellitus, 149
Catarrhal appendicitis, 570, 580
cholangitis, acute, 844
chronic, 852
perforation of gastric ulcer and, 393
cholecystitis, acute, 855
jaundice, 734, 737, 844
stomatitis, 253
ulcers of intestines, 560
Cavernous angioma of tongue, 268
Cecum, rupture of periappendicular abscess into, 572
Cellulitis in diabetes mellitus, 146
Cellulose, metabolism of, 45
Cerebral hemorrhage, diabetes mellitus and, 121
syphilis, diabetes insipidus and, 171
Cerebrospinal vomiting, 343
Chalk stone, 195
Cheek, actinomycosis of, 266
Chemical process in intestines, 497
Chills, in abscess of liver, 794
in appendicitis, 577
mechanism of, 94
Chlorine, metabolism of, 69
Chloroform poisoning, acute yellow atrophy of liver and, 768
Chlorosis, breath in, 250
gastric ulcer and, 375
Cholangitis, 840
catarrhal, acute, 844
diagnosis of, 846
etiology of, 844
feces in, 846
gall-bladder in, 846
jaundice in, 845
liver in, 846
nausea in, 846
pathology of, 844
prognosis of, 847
pruritus in, 846
pulse in, 846
skin in, 846
spleen in, 846
symptoms of, 845
treatment of, 847
urine in, 845
vomiting in, 846
chronic, 852
diagnosis of, 853
etiology of, 852
gall-stones and, 852
jaundice in, 853
pathology of, 852
prognosis of, 853
symptoms of, 853
treatment of, 853
cholelithiasis and, 869
perforation of gastric ulcer and, 393
relapsing, non-surgical drainage of biliary tract in, 748
suppurative, 849
bacteria and, 849
diagnosis of, 851
from malarial fevers, 851
from suppurative pylephlebitis, 851
etiology of, 849
gall-bladder in, 850
jaundice in, 850
leukocytosis in, 851
liver in, 851
onset of, 850
pain in, 850
pathology of, 850
prognosis of, 851
symptoms of, 850

Cholangitis, suppurative, treatment of, 852
Cholecystitis, abscess of liver and, 792
acute, 853
bacteriology of, 854
catarrhal, 855
consequences of, 858
diagnosis of, 859
from appendicitis, 860
etiology of, 853
fever in, 857
gangrenous, 856
jaundice in, 858
leukocytosis in, 859
membranous, 856
nausea in, 857
pain in, 857
pathology of, 854
perforation in, 859
phlegmonous, 856
prognosis of, 860
pulse in, 859
suppurative, 855
findings in, 856
symptoms of, 856
treatment of, 861
typhoid bacillus in, 854
vomiting in, 857
chronic, 861
bile in, 862
diagnosis of, 862
from gall-stones, 862
etiology of, 861
gall-stones and, 862
pathology of, 862
peritonitis and, 953
prognosis of, 863
roentgen-rays in, 862
symptoms of, 862
treatment of, 863
ulcerative, 856
diagnosis of, from appendicitis, 587
from carcinoma of gall-bladder, 892
Choledopancreatic duct, carcinoma of, 888
pathology of, 890
symptoms of, 892
Cholelithiasis, 864. *See* also Gall-stones.
appendicitis and, 865
associated lesions of, 869
atony of stomach and, 366
bacteriology of, 864
biliary fistulæ in, 878
infection in, treatment of, 882
tract and, 864
carcinoma of gall-bladder and, 892
cholangitis and, 869
common duct in, 875
complications of, 877
crepitus in, 875
cystic duct in, 875
diagnosis of, 879
from abscess of liver, 798
from aneurism of hepatic artery, 754
from appendicitis, 587
Cholelithiasis, diagnosis of, from carcinoma of gall-bladder, 880
of pancreas, 713
from duodenal ulcer, 880
from gastric ulcer, 892
from hyperacidity, 320
roentgen-rays in, 879
diet and, 866
etiology of, 864
fever in, 875
gall-bladder and, 865, 874
hyperacidity and, 317
indigestion in, 871
intestinal obstruction in, 879
jaundice in, 873
liver and, 864
metabolism and, 866
necrosis of pancreas and, 670
neoplasm and, 880
operation in, 885
pain in, 871
pancreatitis and, 877
pathogenesis of, 868
pathology of, 867
pelvic infections and, 865
pericholecystic adhesions and, 877
pregnancy and, 865
prognosis of, 881
puerperal infections and, 865
sequelæ of, 877
symptoms of, 870
treatment of, 881
diet in, 883
prophylactic, 881
surgical, 885
Cholemia in jaundice, 741
Choleperitoneum, 908
Cholera infantum, 551
prognosis of, 551
symptoms of, 551
treatment of, 553
morbus, 541. *See* Cholera nostras.
nostras, 541
abdomen in, 541
diagnosis of, 542
diarrhœa in, 541
etiology of, 541
fever in, 541
onset of, 541
pain in, 541
pathology of, 541
prognosis of, 542
symptoms of, 541
treatment of, 543
vomiting in, 541
Chromaffin system, diabetes mellitus and, 127
Chyliform ascites, 215
Chylous ascites, 899
Cicatricial stenosis of pylorus, 466
stricture of œsophagus, 298
Cinchophen in gout, 206
Circulatory system, gastric ulcer and, 375
Circumpapillary carcinoma of duodenum, 634

Cirrhosis, biliary, diagnosis of, from acute yellow atrophy of liver, 772
from carcinoma of liver, 836
from portal cirrhosis, 818, 830
of liver, arthracotic, 822
cardiac, 777
diabetes mellitus and, 129
diagnosis of, from fatty liver, 763
from passive congestion, 779
from perihepatitis, 787
from tuberculosis of peritoneum, 965
malarial, 821
portal, 801
diagnosis of, from biliary cirrhosis, 818, 830
from carcinoma of stomach, 836
of stomach, 478
Colic, appendicular, 581
biliary, 871
diagnosis of, from appendicitis, 587
from necrosis of pancreas, 679
in calculus of pancreas, 695
in carcinoma of intestines, 636
gall-stone, 871
diagnosis of, 879
intestinal, 513
diagnosis of, from appendicitis, 515, 585
lead, 516
mucous, 644
renal, diagnosis of, from appendicitis, 587
Colitis, 546
diagnosis of, 546
from appendicitis, 585
diarrhœa in, 546
etiology of, 546
fever in, 546
hemorrhage in, 546
membranous, 644
mucous, 239, 644
abdomen in, 645
complications of, 646
constipation in, 645
definition of, 644
in descent of intestines, 996
diagnosis of, 646
diarrhœa in, 645
digestion and, 239
etiology of, 644
intestinal sand in, 646
neurasthenia in, 646
pathology of, 645
prognosis of, 646
symptoms of, 645
treatment of, 647
pain in, 546
pathology of, 546
prognosis of, 547
simple, 546
symptoms of, 546
treatment of, 547
Collapse in diarrhœa, 536
in hemoperitoneum, 908
in obstruction of intestines, 606
Colon, carcinoma of, 635
diseases of, acute peritonitis and, 911
dilatation of, congenital, 531
diagnosis of, from dilatation of stomach, 465
idiopathic, pain in, 531
symptoms of, 531
treatment of, 531
inflammation of, 546. *See* Colitis.
redundancy of, 531
roentgen-ray examination in, 532
symptoms of, 532
treatment of, 532
tumors of, diagnosis of, from carcinoma of stomach, 427
Colorless stools, 503
Coma, diabetic, 150
alcoholic form, 151
collapse from, 151
treatment of, 165
typical, 150
Compression of intestines, 600
obstruction from, 614
stenosis of œsophagus, 298
Concretions, intestinal, obstruction from, 610
Congenital anomalies of liver, 751
cysts of pancreas, 701
deformities of frenum of tongue, 268
dilatation of colon, 531
diverticula of intestines, 627
of œsophagus, 285
fixation of duodenum, 630
hypertrophic stenosis of pylorus, 472, 475
malformations of œsophagus, 284
obliteration of biliary ducts, 839
pylorospasm, 472
splanchnoptosis, 987
stenosis of intestine, obstruction from, 613
stricture of œsophagus, 285
webs of œsophagus, 285
Congestion of bowels, constipation and, 522
of liver, 773
diagnosis of, from fatty liver, 763
passive, digestion and, 239
Conjugal diabetes, 117
Constipation, 519
abdominal muscles and, 525
in acute dilatation of stomach, 460
enteritis, 540
hepatitis, 789
peritonitis, 920
in appendicitis, 576
appetite in, 525
in ascites, 902
atonic, 523
in atony of stomach, 365
auto-intoxication and, 526
bacteria in, 521
in carcinoma of intestines, 636
of pancreas, 711

Constipation in chronic enteritis, 544
gastritis, treatment of, 455
peritonitis, 953, 958
in cirrhosis of liver, 812
complications of, 525
congestion of bowels and, 522
of liver and, 774
definition of, 519
in descent of intestines, 996
diagnosis of, 526
diarrhœa in, 525
dilatation of stomach and, 463
diseases of stomach and, 521
dress and, 522
in duodenal ulcer, 556
etiology of, 519
dietetic, 521
functional, 520, 523
organic, 523
fever in, 525
headache in, 524
in hepatoptosis, 996
in hyperacidity, 318
hypochondriasis in, 524
idiopathic dilatation of colon and, 531
in intestinal colic, 515
intestinal torpor and, 520
in jaundice, 742
latent, 519
in mucous colitis, 645
nausea in, 525
in necrosis of pancreas, 676
in nervous anorexia, 362
dyspepsia, 368
neurasthenia and, 524
in obstruction of intestines, 604
pain in, 524
pathology of, 524
in pericolitis, 564
in phlegmonous gastritis, 440
roentgen-ray findings in, 523
sedentary life and, 522
spastic, 523
in splanchnoptosis, 992
in suppurative pancreatitis, 683
symptoms of, 524
treatment of, 527
diet, 528
exercise, 527
medical, 528
surgical, 530
in volvulus, 620
vomiting in, 525
Constricted liver, 751
Constriction of intestines, 600
Continuous gastromyxorrhœa, 332
Convulsions in diabetes insipidus, 175
Coproliths, 524
Corpulency, 209
Corset liver, 751
Cough in carcinoma of œsophagus, 301
Courvoisier's law, 874
Creatine in protein metabolism, 62
Creatinine in protein metabolism, 62
Crepitus in cholelithiasis, 875
Cricopharyngeal spasmodic stenosis of œsophagus, 297
Crises, gastric, 343
Cutaneous burns, duodenal ulcer and, 558
eruptions in gout, 196
Cystic distention of appendix, 593
duct, cholelithiasis and, 875
obstruction of, 875
Cysticercus cellulosæ of peritoneum, 974
Cystitis in appendicitis, 579
Cysts of liver, 838
diagnosis of, from cysts of pancreas, 706
of mesentery, diagnosis of, from cyst of pancreas, 707
of mouth, 260
necrosis of pancreas and, 679
ovarian, diagnosis of, from ascites, 903
from cyst of pancreas, 707
of pancreas, 679, 698
diabetes mellitus and, 122
of peritoneum, 972
cysticercus cellulosæ, 974
dermoid, 977
embryoma, 977
hydatid, 972
mesenteric, 974
non-parasitic, 972
omental, 976
parasitic, 972
retroperitoneal, 977, 978
sanguineous, 976
urachal, 978
Cytology in acute peritonitis, 915

D

Decubital ulcers of intestines, 561
Deforming perihepatitis, 783
Deformities of liver, 751
of spine, acute dilatation of stomach and, 459
Degeneration, parenchymatous, of liver, 761
Dental sepsis, 247
Dercum's disease, 216
Dermatoses of mouth, 260
Dermoid cyst of mouth, 260
of peritoneum, 977
Detoxifying function of liver, 722
Dextrose, 42
Diabetes, bronze, 123, 820
insipidus, 169
appetite in, 175
cerebral syphilis and, 171
classification of, 169
diagnosis of, 175
etiology of, 169
heredity and, 169
hypothalmic region and, 171
incidence of, 169
idiopathic, 169
kidneys and, 172
pathology of, 174
pituitary gland and, 170
tartrate and, 173
pituitrin in, 176
polyuria in, 174
posterior lobe of pituitary and, 172

Diabetes insipidus, prognosis of, 176
symptoms of, 174
syphilis and, 171
theories of, 172
thirst in, 175
treatment of, 176
tuber cinereum and, 178
tuberculous meningitis and, 172
mellitus, 116
abscesses in, 146
acidosis in, 150
treatment of, 165
acromegaly and, 120
acute, 139
hemorrhagic pancreatitis and, 122
adrenals and, 127
age in, 117
albuminuria in, 145
alkalis in, 166
antiketogenic factors in, 157
appetite in, 140, 175
arteries in, 148
arteriosclerosis and, 138
basal metabolism and, 101
blood in, 137
blood-sugar in, 133
boils in, 146
brain lesions and, 121
breath in, 250
bulimia in, 140
calculi of pancreas and, 122, 695
carbohydrate diet and, 119
carbohydrate-free, diet in, 158
carbuncles in, 146
carcinoma of pancreas and, 122, 710, 712
cardiovascular system in, 138
cataract in, 149
cellulitis in, 146
cerebral hemorrhage and, 121
chromaffin system and, 127
chronic, 139
interstitial pancreatitis and, 122
cirrhosis of liver and, 664
coma in, 150, 151
treatment of, 165
complications of, 146
surgical, 167
treatment of, 165
conjugal, 717
convulsions in, 175
in cyst of pancreas, 122, 706
definition of, 116
diabetes insipidus and, 174
dietary excesses and, 119
in dilatation of stomach, 463
in disease of pancreas, 662
emaciated, 139
encephalomalacia and, 121
endocrine glands and, 121
epilepsy and, 121
etiology of, 116
exophthalmic goitre and, 120
fasting in, 159
Diabetes mellitus, fat, 139
fatty acids in, 157
gall-stone colic and, 120
gangrene in, 147
treatment of, 167
gastro-intestinal tract in, 147
glucose tolerance tests in, 134
glycerine in, 163
gout and, 119, 198
Graves' disease and, 120
heart in, 148
hemiplegia in, 148
heredity and, 117
herpes zoster in, 146
high-fat diet in, 162
hunger and, 130
hyperglycemia in, 135
treatment of, 165
hypophysis and, 128
incidence of, 116
infectious diseases and, 120
insulin in, 125, 164
administration of, 164
dosage of, 164
shock in, 165
intarvin in, 163
interstitial pancreatitis and, 690
iritis in, 149
islands of Langerhans in, 122, 663
ketogenic factors in, 157
kidneys in, 130, 138
lipemia in, 137, 149
lipogenous, 139
liver and, 129, 138
mental strain and, 117
metabolism in, 101, 130, 134, 136
multiple sclerosis and, 121
nervous system and, 120, 139, 148
neuritis in, 148
treatment of, 168
neurotic, 139
obesity and, 117, 119
optic neuritis in, 149
pancreas in, 122, 123, 124, 662, 710
pancreatitis and, 122
paraplegia in, 148
parathyroid glands and, 129
paresis in, 121, 148
pathogenesis of, 136
pathology of, 137
perforating ulcer in, 146
phloridzin in, 130
pneumonia in, 148
polydipsia in, 140
polyphagia in, 140
pregnancy and, 120
treatment of, 168
presbyopia in, 149
prognosis of, 153
prophylaxis in, 154
protein metabolism in, 62
pruritus in, treatment of, 168
pseudo-tabes in, 148
race and, 116
reflexes in, 149
respiratory coefficient in, 135

Diabetes mellitus, respiratory quotient in, 41
retinitis in, 149
severe, 139
skin in, 141, 146
social status and, 117
special senses in, 149
sugar consumption and, 119
symptoms of, 139
syphilis and, 120, 124
tabes dorsalis and, 121
thrombophlebitis in, 147
thirst in, 140
thyroid glands and, 129
trauma, 121
treatment of, 154
dietetic, 155
hygienic, 155
medicinal, 163
spa, 169
tuberculosis in, 138, 148
treatment of, 168
a unity disease, 136
urine in, 142
xanthoma in, 147
renal, 130
Diacetic acid, 50
in diabetes mellitus, 144
Diarrhœa, 532
in achylia gastrica, 359
in active congestion of liver, 774
in acute enteritis, 539
hepatitis, 789
yellow atrophy of liver, 771
in amyloid liver, 764
in appendicitis, 576
bacillus coli communis in, 534
dysenteriæ in, 534
enteritidis in, 535
pyocyaneus in, 535
bacteriology of, 534
in carcinoma of pancreas, 711
in childhood, 547
age and, 548
bacillus coli and, 548
lactis aërogenes and, 548
choleraic, 551
dyspeptic, 549
enterocolitis, 550
diagnosis of, 551
fever in, 550
onset of, 550
pain in, 550
prognosis of, 551
stools in, 550
treatment of, 552
vomiting in, 550
environment and, 549
etiology of, 547
food and, 547
pathology of, 549
season and, 548
simple, 549
symptoms of, 549
treatment of, 551
medicinal, 552
in cholera nostras, 541
Diarrhœa in chronic enteritis, 544
in cirrhosis of liver, 812
in colitis, 546
mucous, 645
collapse in, 536
in constipation, 525
diagnosis of, 536
in dilatation of colon, 531
diseases of heart and, 533
of stomach and, 534
enterocolitis and, 534
etiology of, 532
excessive ingestion of fluids and, 532
food and, 532
in hyperacidity, 318, 534
infections and, 534
in intestinal colic, 512
hemorrhage, 518
indigestion, 534
tuberculosis, 596
ulcer, 562
in jaundice, 742
in mesenteric embolism, 642
thrombosis, 642
morning, 533
mucous, 644
nervous influences and, 533
treatment of, 538
in obstruction of intestines, 605
pain in, 536
in pericolitis, 564
in phlegmonous gastritis, 440
in portal thrombosis, 758
purgatives and, 533
renal disease and, 533
in sprue, 653
in suppurative pancreatitis, 683
pylephlebitis, 759
symptoms of, 535
tenesmus in, 536
in toxic gastritis, 442
treatment of, 536
diet in, 536
medicinal, 537
in tuberculous ulcer of intestine, 596
tubular, 644
in ulcer of intestines, 562
in volvulus, 620
Diet, acute dilatation of stomach and, 460
constipation and, 521
gastric ulcer and, 374
hyperacidity and, 321
Dietary excesses, diabetes mellitus and, 119
Dietl's crises in nephroptosis, 995
Digestion, adaptability in, 226
adhesions and, 242
biliary tract in, 240
blood supply and, 238
of carbohydrates, 45
disharmony in, 240
of fat, 49
functional disturbances of, nature of, 227
structural changes from, 230
disease and, 229
general relations of, 223

Digestion, individuality in, 224
infection and, 238
interrelation of functions in, 225
intestinal flora and, 244
malnutrition and, 243
motor function in, 227
mucous colitis and, 239
organic disease and function in, 229
passive congestion and, 239
psychical states and, 225, 243
relation to other organs, 223
superalimentation and, 242, 243
sympathetic correlation in, 241
traction and, 242
vicarious action in, 226
visceral blood supply and, 238
visceroptosis and, 242
Digestive gastrosuccorrhœa, 328
symptoms in carcinoma of stomach, 415
tract, organic changes from functional disorders, 230
Dilatation of colon, diagnosis of, from dilatation of stomach, 465
idiopathic, 530
of hepatic artery, 753
of intestines, carcinoma and, 632
of œsophagus, diagnosis of, from dilation of stomach, 466
diffuse, 290
idiopathic, 291
in stenosis of pylorus, 475
of stomach, acute, 457
chronic, 461
diagnosis of, from chronic gastritis, 466
from dilatation of colon, 465
of œsophagus, 466
idiopathic, 462
Diphtheritic gastritis, 444
Disaccharides, metabolism of, 44
Distention of appendix, cystic, 593
in carcinoma of intestines, 637
in intestinal indigestion, 512
Diverticula of intestines, 627
Diverticulitis, 629
Diverticulum, Meckel, intestinal obstruction and, 610
of œsophagus, 293
congenital, 285
of Vater, biliary infections through, 842
Double lip, 251
Douglas respiration bag, 27
Dropsy, renal, ascites and, 898
Dry mouth, 276
Duct, choledochopancreatic, carcinoma of, 888
cystic, cholelithiasis and, 875
obstruction of, 875
Duodenal hemorrhage, diagnosis of, 487
ulcer, 404, 554
acidity in, 406, 556
age and, 405
appetite in, 556
burns and, 558
chronic peritonitis and, 952
Duodenal ulcer, complications of, 557
constipation in, 556
diagnosis of, 557
from acute pancreatitis, 558
from aneurism of hepatic artery, 754
from appendicitis, 558
from cholelithiasis, 880
from cirrhosis of liver, 818
from gall-stones, 558
from hyperacidity, 319
from intestinal obstruction, 558
etiology of, 554
hemorrhage in, 406, 556
hypersecretion in, 406
icterus in, 406
latent, 406
number of, 406
pain in, 406, 556
pathogenesis of, 405
pathology of, 554
perforation in, 555, 557
periodicity in, 406
physical examination in, 407
prognosis of, 408
roentgen-ray examination in, 407
rupture of, diagnosis of, from appendicitis, 558, 586
secondary changes in, 555
sex and, 404
site of, 406
subphrenic abscess and, 939
pneumothorax and, 949
symptoms of, 555
treatment of, 558
vomiting in, 406, 556
Duodenitis, necrosis of, pancreas and, 672
Duodenum, carcinoma of, 634
circumpapillary, 634
diagnosis of, from carcinoma of stomach, 426
infrapapillary, 635
suprapapillary, 634
congenital fixation of, 630
contents of, pancreatic enzymes in, 657
perforation of, in necrosis of pancreas, 672
stenosis of, 466
traction on, acute dilatation of stomach and, 458
Dysentery, abscess of liver and, 796
acute hepatitis and, 789
Dyspepsia in ascites, 902
in biliary cirrhosis of liver, 828
chronic, 444
in descent of intestines, 996
in gastric ulcer, 381
intestinal fermentative, 512
nervous, 367
abdomen in, 368
appetite in, 368
constipation in, 368
diagnosis of, 369
from atony of stomach, 366

Dyspepsia, nervous, diagnosis of, from carcinoma of stomach, 369
from chronic gastritis, 369
from dilatation of stomach, 466
from ulcer of stomach, 369
etiology of, 368
neurasthenia in, 368
pathology of, 368
prognosis of, 369
symptoms of, 368
treatment of, 370
Dyspeptic diarrhœa in childhood, 549
Dysphagia in cardiospasm, 349
in foreign bodies in œsophagus, 306
intermittent angiosclerotic, 644
Dyspnœa in acute dilatation of stomach, 460
in perforation of gastric ulcer, 393
Dystrophia adiposo-genitalis, diagnosis of, from obesity, 216

E

Echinococcus cyst of liver, diagnosis of, from cyst of pancreas, 706
Eclampsia, acute yellow atrophy of liver and, 768
Eczema in gout, 196
of lips, 253
of mouth, 262
Emaciation in pancreatitis, 684
in syphilis of stomach, 493
Embolic ulcers of intestines, 559
Embolism, gastric ulcer and, 375
of hepatic artery, 753
veins, 755
of mesenteric arteries, 641
of portal vein, 758
pulmonary, in subphrenic abscess, 946
Embryomas of peritoneum, 977
Empyema, diagnosis of, from subphrenic abscess, 947
of gall-bladder, 856
subphrenic abscess and, 940
Encephalomalacia, diabetes mellitus and, 121
Encysted tuberculosis of peritoneum, 962
Endocarditis, mesenteric embolism and, 641
Endocrine disturbances in obesity, 215
glands, diabetes insipidus and, 170
mellitus and, 121
gastric secretion and, 316
hyperacidity and, 316, 317
obesity and, 209, 210, 215, 216, 221
Endometrial adenomas of intestines, 640
Endophlebitis of hepatic veins, obliterating, 755
of portal veins, 760
Enlargement of spleen in thrombosis of portal vein, 758
Emphysematous liver, 761
Enteralgia, 513, 515
Enteritis, acute, 538
Enteritis, acute, abdomen in, 540
bacteria in, 539
constipation in, 541
definition of, 538
diagnosis of, from appendicitis, 585
diarrhœa in, 539
etiology of, 538
fever in, 540
jaundice in, 540
pain in, 540
pathology of, 539
prognosis of, 542
stools in, 539
symptoms of, 539
treatment of, 542
vomiting in, 540
chronic, 544
Enterocolitis, diarrhœa in childhood and, 550
Enterokinase, 498, 499
Enteroptosis, 986. *See* Splanchnoptosis.
Enterostenosis, 992
Enzymes, inverting, 500
in protein metabolism, 183
Epilepsy, diabetes mellitus and, 121
Epinephrine, administration of, basal metabolism and, 103
in carbohydrate metabolism, 127
Epiploitis, 933
symptoms of, 934
treatment of, 934
Epithelioma, leukoplakia and, 273
Erepsin, 500
Eructation, nervous, 341
Erysipelas of mouth, 262
Exogenous adiposity, 210
Extragastric bleeding, 485
Extrahepatic biliary ducts, carcinoma of, 887
pathology of, 889
symptoms of, 891
subphrenic abscess, 943
Extraperitoneal subphrenic abscess, 943
Exudate in ascites, 898
Eyes in gout, 197, 198

F

Facies in acute peritonitis, 917
Fasting, basal metabolism in, 35
in diabetes mellitus, 159
ketosis in, 35
metabolism and, 31
protein metabolism in, 34
respiratory quotient in, 32
Fat, absorption of, 50
in intestines, 500
digestion of, 49
formation of glucose from, 132, 157
in feces, 659
metabolism of, 47
necrosis, of pancreas, 665
oxidation of, 50
Fatness, 209
Fatty acids, cirrhosis of liver and, 802

Fatty acids in diabetes mellitus, 157
total, 51
ascites, 900
liver, 761
oils, 48
stools, 504
Fecal concretions in appendicitis, 568
masses, intestinal obstruction from, 609
vomiting, 605
Feces, 501
in abscess of liver, 796
acholic, 503
in carcinoma of intestines, 637
in catarrhal cholangitis, 846
chemical composition of, 502
color of, 502
colorless, 503
consistency of, 502
in diarrhœa in childhood, 550
in disease of pancreas, 659
fat in, 504, 659
in gangrenous pancreatitis, 678
in jaundice, 742
inorganic constituents of, 503
microscopic examination of, 503
mucus in, 503
muscle nuclei in, 661
in necrosis of pancreas, 676
odor of, 502
quantity of, 501
reaction of, 502
in tuberculosis of peritoneum, 964
Ferment, fat-splitting, in urine, 668
theory of gout, 189
Fermentative dyspepsia, intestinal, 512
Ferments in carcinoma of stomach, 420
Fever in abscess of liver, 794
in acute cholecystitis, 857
enteritis, 540
hepatitis, 789
peritonitis, 921
yellow atrophy of liver, 771
in aneurism of hepatic artery, 754
in appendicitis, 576
basal metabolism and, 100
in carcinoma of gall-bladder, 890
of pancreas, 713
of stomach, 417
cause of, 98
in cholelithiasis, 875
in cholera nostras, 541
in cirrhosis of liver, 812, 829
in colitis, 546
in constipation, 525
in diarrhœa in childhood, 550
in gangrenous pancreatitis, 678
hepatic intermittent, 876
metabolism in, 98
in necrosis of pancreas, 676
in phlegmonous gastritis, 439
in subphrenic pyopneumothorax, 950
in suppurative pancreatitis, 683
in tuberculosis of peritoneum, 964
in ulcer of intestines, 562
Fibrinopurulent peritonitis, 914
Fibroma of peritoneum, 969
Fibroma of tongue, 274
Fibromyoma of peritoneum, 969
Fistulæ, biliary in cholelithiasis, 878
Flagellata in carcinoma of stomach, 422
Flatulence in carcinoma of stomach, 415
in intestinal indigestion, 512
Focal infection of mouth, 247
Follicular ulcers of intestines, 560
Food, absorption of, in intestines, 500
diarrhœa and, 532
in childhood and, 547
fear of, 363
specific dynamic action of, 82
Foods, acid, 71
metabolism and, 29
Foodstuffs, metabolism of, 37
Foot and mouth disease, mouth in, 263
Foramina ventriculi nervosa, 355. *See* Peristaltic unrest.
Foreign bodies in appendicitis, 568
dilatation of stomach and, 462
intestinal obstruction from, 610
in œsophagus, 303
stenosis of pylorus and, 467
Frenum of tongue, deformities of, 268
ulcer of, 271
Function of liver, bactericidal, 724
bile secreting, 716
detoxifying, 722
disorders of, 715
glycogenic, 719
in iron metabolism, 725
lipogenetic, 725
urea-forming, 721
Functional disturbances, intestinal colic and, 513
hiatal stenosis, 291
paralysis of intestines, obstruction from, 625

G

Gall-bladder, adhesions of, 877
anomalies of, 839
carcinoma of, 886
ascites in, 891
diagnosis of, 892
from carcinoma of liver, 892
from cholecystitis, 892
from cholelithiasis, 880
jaundice in, 891
liver and, 889
pain in, 890
pancreas and, 712
pathology of, 888
symptoms of, 890
treatment of, 893
in catarrhal cholangitis, 846
in cholelithiasis, 865, 874
in chronic peritonitis, 957
cirrhosis of liver and, 806
diseases of, acute peritonitis and, 911
empyema of, 856
perforation of, diagnosis of, from necrosis of pancreas, 679
in suppurative cholangitis, 850

Gall-bladder, tumors of, diagnosis of, from carcinoma of stomach, 427
dilatation of stomach and, 462
wall of, biliary infection through, 841
Gall-stone colic, 871
diabetes mellitus and, 120
diagnosis of, 879
nausea in, 871
pain in, 871
treatment of, 883
vomiting in, 878
Gall-stones, 864. *See* also Cholelithiasis.
character of, 875
chronic cholangitis and, 852
cholecystitis and, 862
in common duct, 875
in cystic duct, 875
diagnosis of, from cholecystitis, 862
from duodenal ulcer, 558
from gastric ulcer, 391
from nervous gastralgia, 336
discharge of, 882
in diverticulum of Vater, 875
formation of, 868
glycosuria and, 120
infection with, treatment of, 882
intestinal obstruction from, 609, 879
latency of, 870
situation of, 868
solution of, 882
results of, 869
varieties of, 867
Gall-tract disease, diagnosis of, difficulties in, 743
present conception of, 743
therapeutic status of, 743
vicious circles of, 744
Ganglionated neuroma of peritoneum, 970
Gangrene of appendix, 571
in diabetes mellitus, 147
of pancreas, necrosis and, 678
Gangrenous appendicitis, 580
cholecystitis, 856
stomatitis, 256
Gaseous distention of intestines, 509
liver, 761
Gastralgia nervosa, 335
diagnosis of, 336
from carcinoma of stomach, 336
from chronic gastritis, 336
from gall-stones, 336
from gastric ulcer, 390
from intercostal neuralgia, 336
from intestinal colic, 336
from nephritic colic, 336
etiology of, 335
in mycotic gastritis, 442
nausea in, 335
pain in, 335
symptoms of, 335
treatment of, 336
vomiting in, 335
Gastralgokenosis, 334
Gastrectasis, 456. *See* Stomach, dilatation of.
Gastric anacidity, 357. *See* Achylia gastrica.
analysis in carcinoma of stomach, 419
in gastric ulcer, 385
in syphilis of stomach, 493
atony, 364, 456
nervous system and, 456
bleeding, 484
contents in achylia gastrica, 359
in atony of stomach, 366
in chronic gastritis, 451
crises, 343
diagnosis of, from dilatation of stomach, 466
disease, carcinoma and, 410
emptiness, painful, 334
hyperesthesia, 337
diagnosis of, 338
etiology of, 337
symptoms of, 337
treatment of, 338
idiosyncrasies, 338
juice, hypersecretion of, 323. *See* Gastrosuccorrhœa.
secretion of, 235
neurasthenia, 367
neuroses, 307
age in, 311
classification of, 312
definition of, 307
diagnosis of, 312
from chronic gastritis, 453
etiology of, 310
occurrence of, 310
prognosis of, 313
treatment of, 313
regurgitation, diagnosis of, 340
etiology of, 340
prognosis of, 341
symptoms of, 340
treatment of, 340
rigidity in carcinoma of stomach, 418
ulcer, 371. *See* also Stomach, ulcer of
age in, 373
alkalies in, 401
anemia and, 375
antibodies and, 376
arterial spasm and, 375
backache in, 381
carcinoma and, 394, 410
developing upon, 394
diagnosis of, 395
symptoms of, 395
of stomach and, 410
cardiac stenosis and, 395
chlorosis and, 375
chronic peritonitis and, 952
cicatrization in, 380
circulatory system and, 375
complications of, 391
course of, 397
definition of, 371
diagnosis of, 389
from appendicitis, 391
from carcinoma, 390
from cholelithiasis, 892
from cirrhosis of liver, 819

Gastric ulcer, diagnosis of, from gallstones, 391
from gastralgia, 390
from gastritis, 390
from hyperacidity, 319
from nervous dyspepsia, 369
diet and, 374
distribution of, 372
dyspepsia in, 381
embolism and, 375
etiology of, 372
gastric analysis in, 385
healing of, 380
hematemesis in, 383, 488
hemorrhage in, treatment of, 403
histology of, 380
hour-glass stomach and, 396
treatment of, 404
hyperacidity and, 376
hypermotility in, 387
hypersecretion and, 376
infarction and, 372, 375
intestinal hemorrhage and, 518
latent, 381
nervous system and, 376
number of, 378
"occult bleeding" in, 384
occupation in, 374
pain in, 382
treatment of, 400
parotitis in, 395
pathogenesis of, 372
pathology of, 378
perforation of, 392
catarrhal cholangitis and, 393
into abdominal wall, 393
into intestines, 393
into spleen, 393
pain in, 393
signs of, 393
symptoms of, 393
treatment of, 403
perigastritis in, 391
symptoms of, 392
prognosis of, 397
pseudoperforation of, 394
pyloric stenosis and, 395
roentgen-ray examination in, 386
rupture of, diagnosis of, from appendicitis, 586
scars in, 381
secretion in, 377
sequelæ of, 391
sex in, 373
shape of, 380
signs in, 385
situation of, 378
size of, 380
spasm in, 377, 400
subphrenic abscess and, 939
pyopneumothorax and, 949
symptoms of, 381
tetany and, 395
trauma and, 374
treatment of, 398
ambulatory, 402
Gastric ulcer, treatment of, diet in, 399
medicinal, 398
rest in, 399
surgical, 402
urine in, 382
vomiting in, 382
Gastritis, acid, diagnosis of, from hyperacidity, 320
acute, 434
classification of, 434
diagnosis of from appendicitis, 585
simple, 434
constipation in, treatment of, 438
definition of, 434
diagnosis of, 437
diarrhœa in, treatment of, 438
etiology of, 434
jaundice in, 436
nausea in, 436
treatment of, 438
pain in, 436
pathology of, 435
primary, 434
prognosis and, 437
secondary, 435
signs of, 436
prophylaxis in, 437
symptoms of, 436
treatment of, 437
vomiting in, 436
treatment of, 438
chronic, 444
achylia in, 451
alcoholism and, 446
anorexia in, 450
atrophic, 450
cirrhosis of stomach and, 450
classification of, 445
constipation in, treatment of, 455
definition of, 444
diagnosis of, 452
from achylia gastrica, 453
from carcinoma of stomach, 425, 453
from dilatation of stomach, 466
from gastralgia, 336
from gastric neuroses, 453
from nervous dyspepsia, 369
gastralgia, 336
etiology of, 446
gastric contents in, 451
hyperacidity in, 451
incidence of, 444
intestines in, 450
nausea in, 450
nutrition in, 450
pathology of, 447
pepsin in, 451
productive, 447
prognosis of, 452
prophylaxis in, 453
rennet ferment in, 451
symptoms of, 450

Gastritis, chronic, treatment of, 453
dietetic, 454
mechanical, 453
medicinal, 455
vomiting in, 450
cystica, 447
diagnosis of, from gastric ulcer, 390
diphtheritic, 444
interstitial purulent, 438
membranacea, 444
mucous, 445
mycotic, 442
etiology of, 443
gastralgia in, 443
hyperchlorhydria in, 443
symptoms of, 443
treatment of, 444
vomiting in, 443
phlegmonous, 438
age in, 439
circumscribed, 440
constipation in, 440
definition of, 438
diagnosis of, 440
diarrhœa in, 440
diffuse, 439
etiology of, 438
fever in, 439
nausea in, 440
pain in, 440
pathology of, 439
prognosis of, 440
sex in, 439
symptoms of, 439
treatment of, 440
vomiting in, 440
proliferative, 447
secondary, 447
stenosing, 467
toxic, 441
diagnosis of, 442
diarrhœa in, 442
etiology of, 441
jaundice in, 442
pain in, 442
petechiæ in, 442
prognosis of, 442
symptoms of, 441
treatment of, 442
urine in, 442
vomiting in, 442
Gastro-intestinal splanchnoptosis, 993
tract in cirrhosis of liver, 809
in diabetes mellitus, 147
in jaundice, 742
Gastro-jejunal ulcer of intestines, 559
Gastromyxorrhœa, 330
continuous, 332
intermittent, 331
Gastroptosis, 991
in atony of stomach, 366
diagnosis of, 997
from dilatation of stomach, 466
incidence of, 991
symptoms of, 993
treatment of, 1001
Gastrosuccorrhœa, 323
Gastrosuccorrhœa continua chronica, 325
diagnosis of, 327
etiology of, 326
pathology of, 326
prognosis of, 327
sequelæ of, 327
symptoms of, 326
treatment of, 328
periodica, 323
diagnosis of, 324
etiology of, 324
prognosis of, 325
symptoms of, 324
treatment of, 325
vomiting in, 324
digestive, 328
diagnosis of, 330
etiology of, 329
gastric contents in, 329
prognosis of, 330
symptoms of, 329
treatment of, 330
periodic hypersecretion in, 325
in pylorospasm, 353
Gastroxynsis, 324
Geographical tongue, 271
Glaucoma in gout, 198
Glénard's disease, 986. *See* Splanchnoptosis.
Glossitis, 270
chronic superficial, 271
streptococcal, 270
Moeller's, 271
papillaris, 271
papillosa acuta, 271
symptoms of, 270
treatment of, 270
Glossodynia, 272
exfoliative, 271
Glossoplegia, 269
Glucose, 42
forms of, 132
formation of, from carbohydrate, 131, 157
from fat, 132, 157
from protein, 131, 157
molecule, 132
tolerance test, 47, 134
in urine, tests for, 143
Glukokinin, 126
Glycerol, metabolism of, 49
Glycogen, metabolism of, 44
in urine in diabetes mellitus, 146
Glycogenase, 131
Glycogenic function of liver, 719
Glycosuria, alimentary, 133
pancreas and, 664
in calculus of pancreas, 696
in carcinoma of pancreas, 712
cerebral hemorrhage and, 121
disease of pancreas and, 661
gall-stones and, 120
in gangrenous pancreatitis, 678
in gout, 198
in interstitial pancreatitis, 691
in necrosis of pancreas, 676
nervous system and, 120

Glycosuria, renal, 130
in suppurative pancreatitis, 684
trauma and, 121
tumors of brain and, 121
Glycuronic acid in urine in diabetes mellitus, 144
Goitre, exophthalmic, diabetes mellitus and, 120
Gonad adiposity, 215
obesity, 215
Gonococcus, peritonitis from, 924
stomatitis, 259
Gout, 178
acute, 194
age and, 179
albuminuria in, 197
alcohol and, 179
alimentary disorders in, 196
alloxuric bodies in, 181
arteriosclerosis in, 193, 197
arthritis in, 191, 194
asthma in, 197
atophan in, 206
blood in, 190
cardiovascular lesions in, 193
chronic, 194
cinchophen in, 206
complications of, 197
treatment of, 208
cutaneous eruptions in, 196
definition of, 178
diabetes mellitus and, 119, 198
diagnosis of, 198
from arthritis deformans, 200
roentgen-rays in, 199
eczema in, 196
etiology of, 178
exercise and, 179
eyes in, 197, 198
food and, 179
glaucoma in, 198
glycosuria in, 198
headache in, 196
heart in, 197
Heberden's nodes in, 195
heredity and, 178
incidence of, 178
iritis in, 198
irregular, 195
diagnosis of, 200
joints in, 191
kidneys in, 188, 193
lead poisoning and, 180
metabolism in, 180
migraine in, 196
myocarditis in, 197
nephritis in, 198
nervous manifestations in, 196
neuralgia in, 196
occupation and, 180
pathology of, 190
pericarditis in, 198
phlebitis in, 198
physique and, 180
primary articular, 193
renal, 193
prognosis of, 201
Gout, race and, 179
respiratory system in, 193
retrocedent, 198
sciatica in, 196
sex and, 179
skin in, 196
symptoms of, 194
theories of, 188
ferment, 189
nervous, 189
pathological accentuation of renal insensitiveness, 190
primary tissue change, 189
renal, 189
tissue retention, 190
tissue necrosis in, 191
tophi in, 192, 199
trauma and, 180
treatment of, 201
alkalies in, 204
dietetic, 202
electricity in, 207
hygienic, 201
medicinal, 205
mineral waters in, 204
operative, 207
prophylactic, 201
urate crystals in, 199
deposits in, 191, 194
uremia in, 198
uric acid in blood in, 186
excretion of, 187
metabolism in, 186
solvents of, 207
urine in, 197
Gouty diathesis, 195
Graves' disease, diabetes mellitus and, 120
Granulomata of œsophagus, 288
Growth, metabolism and, 91
Gums, tuberculosis of, 264

H

Habitual constipation, 519
Halitosis, 248
Hanot's cirrhosis of liver, 799, 826
Harelip, 253
Headache in constipation, 524
in gout, 196
Heart in cirrhosis of liver, 810
in congestion of liver, 777
in diabetes mellitus, 148
diseases of, diarrhœa and, 533
intestinal hemorrhage and, 517
in gout, 197
in jaundice, 740
in obesity, 211
Heartburn in hyperacidity, 317
Heberden's nodes in gout, 195
Hemangioma of intestines, 640
Hematemesis, 484
in acute yellow atrophy of liver, 771
age in, 485
in carcinoma of stomach, 416
in cirrhosis of liver, 812
treatment of, 824

Hematemesis, definition of, 484
diagnosis of, 486
from carcinoma of œsophagus, 487
of stomach, 488
from duodenal hemorrhage, 487
from erosions, 488
from miliary aneurisms, 488
from ulcer of stomach, 488
from varices of œsophagus, 487
in stomach, 488
from venous stasis, 488
from vicarious hemorrhages, 488
etiology of, 484
extragastric, 485
gastric, 484
in gastric ulcer, 383
neuropathic, 488
pathology of, 485
prognosis of, 489
prophylaxis in, 490
sex in, 485
in suppurative pylephlebitis, 759
symptoms of, 485
in syphilis of stomach, 493
in thrombosis of portal vein, 758
treatment of, 489
accessory, 490
surgical, 490
Hematogenous jaundice, 732
Hematoma, retroperitoneal, 977
Hematuria in nephroptosis, 995
Hemiplegia in diabetes mellitus, 148
Hemochromatosis, 123, 765
interstitial pancreatitis and, 690
pathology of, 766
portal cirrhosis of liver and, 820
treatment of, 766
Hemofuscin in liver, 766
Hemolytic jaundice, 732
Hemoperitoneum, 907
collapse in, 908
diagnosis of, 908
pain in, 908
prognosis of, 908
sequelæ of, 908
symptoms of, 908
treatment of, 908
vomiting in, 908
Hemoptysis, breath in, 250
Hemorrhage in acute yellow atrophy of liver, 771
in aneurism of hepatic artery, 754
cerebral, diabetes mellitus and, 121
in cirrhosis of liver, 766
in colitis, 546
in duodenal ulcer, 401, 556
diagnosis of, 487
from tongue, 269
in gastric ulcer, 383
treatment of, 403
intestinal, 517
in portal thrombosis, 757
into pancreas, 668
in mesenteric embolism, 642
thrombosis, 642
in ulcer of intestines, 562
Hemorrhage, vicarious, diagnosis of, 488
Hemorrhagic necrosis of pancreas, 668
pancreatitis, diagnosis of, from acute peritonitis, 926
Hemorrhoids, intestinal hemorrhage and, 517
Hemosiderin in liver, 766
Henoch's purpura, diagnosis of, from appendicitis, 588
Hepatic anthracosis, 764
artery, abscess of liver and, 791
aneurism of, 754
diagnosis of, 754
from cholelithiasis, 754
from duodenal ulcer, 754
fever in, 754
hemorrhage in, 754
jaundice in, 754
pain in, 754
pathology of, 754
symptoms of, 754
treatment of, 754
dilatation of, 753
embolism of, 753
thrombosis of, 753
intermittent fever, 876
jaundice, 732
silicosis, 764
splanchnoptosis, 993
veins, abscess of liver and, 791
chronic obliterating endophlebitis of, 755
dilatation of, 755
embolism of, 755
thrombosis of, 755
suppurating phlebitis of, 755
thrombophlebitis of, 755
Hepatitis, acute, 787
non-suppurative, 788
alcoholism and, 788
constipation in, 789
diagnosis of, 789
diarrhœa in, 789
dysentery and, 789
etiology of, 788
fever in, 789
jaundice in, 789
liver in, 789
malarial fever and, 788
pain in, 789
pathology of, 788
prognosis of, 790
spleen in, 789
symptoms of, 789
treatment of, 790
urine in, 789
vomiting in, 789
parenchymatous, 788
chronic interstitial, 799. *See* Liver, cirrhosis of.
suppurative, 790. *See* Liver, abscess of.
Hepatogenous jaundice, 732
Hepato-lenticular degeneration, 831
Hepatoptosis, 753, 995
constipation in, 996
diagnosis of, 998

Hepatoptosis, meteorism in, 996
pain in, 996
symptoms of, 996
Hepatopulmonary abscess, 796
Hernia, diaphragmatic, diagnosis of, from subphrenic pyopneumothorax, 952
external, intestinal obstruction from, 611
internal, intestinal obstruction from, 611
intestinal hemorrhage and, 517
Herpes buccalis, 259
labialis, 252
of œsophagus, 289
zoster in diabetes mellitus, 146
Herpetic stomatitis, 259
Hexoses, 42
Hiatal œsophagismus, 291
Hiccough in acute perihepatitis, 781
peritonitis, 920
Hippocratic fingers in biliary cirrhosis of liver, 829
Hippuric acid in protein metabolism, 63
Hirschsprung's disease, 530
Hobnail liver, 804
Hour-glass stomach, 396
Hunger, abnormal, 333
diabetes, 130
Hutchinson's teeth, 266
Hyaline perihepatitis, 783
Hydatid cyst of liver, subphrenic pyopneumothorax and, 949
of pancreas, 701
of peritoneum, 972
disease, diagnosis of, from carcinoma of liver, 837
Hydrogen-ion concentration in diabetes mellitus, 152
Hydronephrosis in carcinoma of liver, 835
Hyperacidity, 314
appendicitis and, 317
appetite in, 318
atony and, 319
cholelithiasis and, 317
in chronic gastritis, 451
constipation in, 318
diagnosis of, 319
diarrhœa in, 318, 534
digestive period in, 315
endocrine glands and, 316, 317
eructations in, 317
etiology of, 316
gastric juice in, 318
heartburn in, 317
interdigestive period in, 315
mental conditions and, 317
pain in, 317
pathology of, 317
prognosis of, 320
symptoms of, 317
treatment of, 320
ulcer of stomach and, 316
urine in, 319
vomiting in, 319
Hyperalgesia in appendicitis, 575
Hyperchlorhydria, 314. *See* Hyperacidity
foods exciting, 321
Hyperchlorhydria, mycotic gastritis and, 443
Hyperesthesia gastrica, 337. *See* Gastric hyperesthesia.
of mouth, 251
Hyperglycemia, diabetes mellitus and, 135
treatment of, 165
Hyperkeratosis of tongue, 269
Hyperplasia in cirrhosis of liver, 808
Hyperplastic intestinal tuberculosis, 597
perihepatitis, chronic, 783
Hyperptyalism, 276
Hypersecretion, diagnosis of, from dilatation of stomach, 466
from hyperacidity, 319
diet in, 320
in duodenal ulcer, 406
gastric, chronic, 325
digestive, 328
of mucus, 330
periodic, 323
diagnosis of, from gastrosuccorrhœa, 325
ulcer and, 376
Hyperthyroidism, metabolism and, 103
Hypertrophic biliary cirrhosis, of liver, 826
stenosis of pylorus, 230
congenital, 472
diagnosis of, from carcinoma of stomach, 428
infantile, 472
Hypertrophy of islands of Langerhans, 663
Hyphomycetic stomatitis, 258
Hypochlorhydria, 356
diagnosis of, 357
symptoms of, 356
treatment of, 357
Hypochondriasis in constipation, 524
Hypophysis, carbohydrate metabolism and, 128
diabetes insipidus and, 170
mellitus and, 128
Hypostasis, 992
Hypotyalism, 276
Hysteria, cardiospasm and, 348
diagnosis of, from appendicitis, 588
nervous anorexia and, 362

I

Ichthyosis buccalis, 272
Icterus, 731. *See* Jaundice.
index, 728
neonatorum, 737
Idiopathic diabetes insipidus, 169
dilatation of colon, 530
peritonitis, primary, 910
Ileum, carcinoma of, 635
Ileus, 600
Imperfect œsophagus, 285
Inanition, chronic, metabolism in, 36
Incarceration of intestines, 600
obstruction from, 613
Incontinence of pylorus, 364
Indigestion, intestinal, 511
diarrhœa and, 534

Indigestion in splanchnoptosis, 992
Infantile hypertrophic stenosis of pylorus, 472
Infantilism, pancreas and, 664
Infarction, gastric ulcer and, 375
intestinal hemorrhage and, 517
Infection, dental, 247
digestion and, 238
focal, gastric ulcer and, 372
of mouth, 247
Inflammation of colon, 546. *See* Colitis.
of labial glands, 253
of mouth, 253
of œsophagus, 285
of parotid glands, 277
Infrapapillary carcinoma of duodenum, 635
Ingluviosis, 291
Innervation, contrary, in intestine, 310
Insulin, chemistry of, 126
history of discovery of, 125
shock, 165
sources of, 126
standardization of, 125
in treatment of diabetes mellitus, 164
administration of, 164
dosage of, 164
Intarvin in diabetes mellitus, 613
Interacinar pancreatitis, 689
Intercostal neuralgia, diagnosis of, from nervous gastralgia, 336
Interlobular pancreatitis, 689
Intermittent gastromyxorrhœa, 331
Internal secretions, obesity and, 210
Interstitial hepatitis, chronic, 799
pancreatitis, 686
purulent gastritis, 438
Intestinal colic, 513
constipation in, 515
definition of, 513
diagnosis of, 515
from appendicitis, 515, 585
from nervous gastralgia, 336
diarrhœa in, 512
etiology of, 513
functional disturbances and, 513
nausea in, 515
organic conditions and, 514
pain in, 514
symptoms of, 514
treatment of, 516
vomiting in, 515
concretions, obstruction from, 610
fermentative dyspepsia, 512
flora, digestion and, 244
hemorrhage, 517
amyloid degeneration and, 517
anemia and, 517
ankylostoma and, 517
cardiac disease and, 517
congestive condition of bowels and, 517
diarrhœa in, 518
diseases of bloodvessels and, 517
duodenal ulcer and, 518
embolism of mesenteric vessels and, 517
Intestinal hemorrhage, etiology of, 517
gastric ulcer and, 518
hemorrhoids and, 517
hernia and, 517
infarction of bowel and, 517
inflammatory conditions of bowel and, 518
intussusception and, 517
prognosis of, 518
stools in, 518
strangulation of bowel and, 517
symptoms of, 518
thrombosis of mesenteric vessels and, 517
of portal vein and, 757
treatment of, 518
ulcerative condition of bowel and, 518
unassociated with pathological conditions of bowel, 517
indigestion, 511
diagnosis of, 512
diarrhœa and, 534
etiology of, 511
fermentative, 512
symptoms of, 512
treatment of, 512
processes, automatic mechanism in, 501
sand, 504
in mucous colitis, 646
torpor, constipation and, 520
tract, bacteriology of, 504
physiology of, 495
Intestines, absorption of carbohydrates in, 500
of fats in, 500
of food in, 500
adenoma of, 639
adhesions of, carcinoma and, 633
amyloid disease of, 599
antiperistalsis of, 496
pathological, 497
arteriosclerosis of, 643
bacillus acidophilus in, 505
aërogenes, capsulatus in, 505
bifidus comminis in, 505
bulgaricus in, 509
coli in, 505
lactis aërogenes in, 505
putrifiens in, 505
bacteria in, distribution of, 505
growth of, 506
significance of, 506
treatment of, 508
types of, diagnosis of, 507
virulence of, 506
carcinoma of, 631
adhesions and, 633
anemia in, 637
blood in, 637
colic in, 636
complications of, 637
constipation in, 636
dilatation and, 632
distention in, 637
feces in, 637

Intestines, carcinoma of, metastasis and, 633
obstruction and, 632
pathology of, 632
perforation in, 633
peritonitis and, 633
pus in, 637
symptoms of, 634
treatment of, 638
tumors in, 636
chemical processes in, 497
in chronic gastritis, 451
compression of, 600
constriction of, 600
contractions of, tonic, 497
contrary innervation in, 310
descent of, 996
dilatation of, carcinoma and, 632
diseases of, 495
acute peritonitis and, 911
diverticula of, 627
acquired, 628
congenital, 627
false, 628
symptoms of, 630
treatment of, 630
true, 628
as excretory organs, 500
gaseous distention of, 509
diagnosis of, 510
symptoms of, 510
treatment of, 511
hemangioma of, 640
incarceration of, 600
lipoma of, 640
lymphangioma of, 640
lymphosarcoma of, 638
symptoms of, 639
treatment of, 639
motor functions of, 495
movements of, mechanism of, 496
nervous, 496
mucosal, 497
myoma of, 640
neuralgia of, 513, 515
obstruction of, 600
acute, 601
carcinoma and, 632
in cholelithiasis, 879
chronic, 600
collapse in, 606
constipation in, 604
definition of, 600
diagnosis of, 607
from acute peritonitis, 926
from appendicitis, 586
from ascites, 903
from duodenal ulcer, 558
from gall-stones, 621
roentgenological, 609
situation of, 608
urine in, 609
diarrhœa in, 605
from adhesions, 613
from bands, 610
from compression of bowel, 614
from concretions, 610
Intestines, obstruction of, from external hernia, 611
from fecal masses, 609
from foreign bodies, 610
from gall-stones, 609
from incarceration of bowels, 613
from internal hernia, 611
from intussusception, 615
age and, 616
etiology of, 615
location of, 616
pain in, 618
pathology of, 616
prognosis of, 618
symptoms of, 617
tenesmus in, 618
treatment of, 618
from knotting, 618. *See* Volvulus.
from Meckel diverticulum, 610
from paralysis of bowel, 625
functional, 625
symptoms of, 626
treatment of, 626
with organic disease, 626
from peritoneal adhesions, 613
from stenosis, 614
from stricture, 613
treatment of, 614
from twisting, 618. *See* Volvulus.
meteorism in, 604
pain in, 603
pathology of, 600
in portal thrombosis, 758
prognosis of, 622
prostration in, 606
symptoms of, 603
toxemia and, 601
treatment of, 622
surgical, 624
vomiting in, 605
obturation of, 600
perforation of, carcinoma and, 633
in gastric ulcer, 393
peristalsis of, 495
pathological, 497
varieties of, 497
physiology of, 495
ptosis of, 996
rhythmic segmentation in, 495
sarcoma of, 638
blood in, 639
fever in, 639
symptoms of, 639
treatment of, 639
strangulation of, 600
stricture of, 600
syphilis of, 598
symptoms of, 598
treatment of, 599
tuberculosis of, 594
chronic hyperplastic, 597
perforation in, 595
stenosing, 596
treatment of, 597

Intestines, tuberculosis of, ulcerative, 595
diagnosis of, 596
diarrhœa in, 596
symptoms of. 596
terminal changes in, 595
tumors of, benign, 939
symptoms of, 640
treatment of, 641
malignant, 631
ulcer of, 553
catarrhal, 560
decubital, 561
diagnosis of, 563
diarrhœa in, 562
duodenal, 554
embolic, 559
fever in, 562
follicular, 560
gastro-jejunal, 559
hemorrhage in, 562
leukemic, 561
pain in, 562
prognosis of, 563
stercoral, 561
symptoms of, 561
thrombotic, 559
treatment of, 563
trophic, 561
uremic, 559
Intraperitoneal subphrenic abscess, 941
Intussusception, 615
intestinal hemorrhage and, 517
obstruction from, 615
Inverting enzymes, 500
Iodine, metabolism of, 70
Iritis in diabetes mellitus, 149
in gout, 198
Iron, metabolism of, 69
Islands of Langerhans, diabetes mellitus and, 122, 663
hypertrophy of, 663

J

Jackson's veil in descent of intestines, 996
Jaundice, 731
in abscess of liver, 794
acquired, 738
in acute cholangitis, 845
cholecystitis, 858
enteritis, 540
gastritis, 436
hepatitis, 789
yellow atrophy of liver, 770
in aneurism of hepatic artery, 754
blood in, 739
bloodvessels in, 740
bradycardia in, 740
in calculus of pancreas, 695
in carcinoma of gall-bladder, 891
of liver, 834
of pancreas, 712
catarrhal, 734, 737, 844
non-surgical drainage of biliary tract in, 749
pathogenesis of, 737
Jaundice in cholelithiasis, 873
cholemia in, 741
chronic splenomegalic hemolytic, 737
in chronic cholangitis, 853
peritonitis, 953
in cirrhosis of liver, 813, 828
of stomach, 483
in congestion of liver, 774
constipation in, 742
in cyst of pancreas, 705
diarrhœa in, 742
dissociated, 732
in duodenal ulcer, 406
effect of, on liver, 738, 740
feces in, 742
in gangrenous pancreatitis, 678
gastro-intestinal tract in, 742
heart in, 740
hematogenous, 732
hemolytic, 732, 737
hepatic, 732
infective, 732, 736
pathogenesis of, 736
toxic, 732, 737
latent, 732
liver in, 740
mechanism of, 735
mucous membrane in, 738
necrosis of pancreas and, 676
nervous system in, 741
in new-born, 737
nutrition in, 742
obstructive, 731, 732, 736
non-surgical drainage of, biliary tract in, 748
pathogenesis of, 736
pathogenesis of, 735
pruritus in, 739
skin in, 738
in suppurative cholangitis, 850
pancreatitis, 683
telangiectasis in, 739
toxic, 732
pathogenesis of, 736
in tuberculosis of peritoneum, 965
types of, 732
urine in, 740
urobilinuria in, 740
urticaria in, 739
Jaw, actinomycosis of, 266
Jejunum, carcinoma of, 635
Joints in gout, 191
Jones' liver functional tests, 729
metabolimeter, 27
Juvenile vomiting, 345

K

Keratosis buccalis, 273
Ketogenic factors in diabetes mellitus, 157
Ketones, metabolism of, 50
Ketonuria, 73
Ketoses, 42
Ketosis, 51, 73, 136, 150
in fasting, 35

Kidney, acute dilatation of stomach and, 460
in cirrhosis of liver, 810
in diabetes insipidus, 172
mellitus, 130, 138
diseases of, diarrhœa and, 533
in gout, 193
movable, diagnosis of, from appendicitis, 588
in obesity, 211
King respiration apparatus, 27
Krogh respiration apparatus, 27
Kupffer cells, bile and, 736

L

Labial glands, inflammation of, 253
Lacrimal glands, enlargement of, 281
Lactescent ascites, 900
Lactic acid in carcinoma of stomach, 420
Lactose, metabolism of, 44
Laennec's cirrhosis of liver, 799
Lane's bands in descent of intestines, 996
Langerhans, islands of, diabetes mellitus and, 122, 663
Larynx, carcinoma of, breath in, 250
Lead colic, 516
poisoning, gout and, 180
Leprosy of mouth, 267
Leukemia, enlargement of liver in, diagnosis of, from fatty liver, 763
infiltration of liver in, 766
mouth in, 263
ulcers of intestines in, 561
Leukocytosis in abscess of liver, 796
in acute cholecystitis, 859
in appendicitis, 577
in gangrenous pancreatitis, 678
in necrosis of pancreas, 676
in subphrenic pyopneumothorax, 950
in suppurative cholangitis, 851
pancreatitis, 684
in tuberculosis of peritoneum, 964
Leukoplakia, 272
epithelioma and, 273
etiology of, 272
pathology of, 273
symptoms of, 273
syphilis and, 272
treatment of, 273
Leukoplasia, 272
Levulose, 42
Levulosuria in hepatic disease, 719
Lichen planus of mouth, 261
Lingua nigra, 269
Linguo-papillitis, 271
Lip, double, 251
eruptions of, 252
Lipase, 499
Lipemia in diabetes mellitus, 137
retinalis, 149
Lipins, metabolism of, 48
Lipogenetic function of liver, 725
Lipoma of intestines, 640
of peritoneum, 970
Lipomatosis universalis, 209
Lips, actinomycosis of, 266
color of, 252
double, 251
dryness of, 252
eczema of, 253
eruptions of, 252
treatment of, 253
fissure of, 252
herpes of, 252
treatment of, 253
shape of, 252
tremor of, 252
tuberculosis of, 264
tumors of, 253
Lipuria in diabetes mellitus, 146
Lithemia, 195
Lithemic splanchnoptosis, 993
Liver, abscess of, 790
amœbic, 793
appendicitis and, 791
bacteria in, 790
biliary ducts and, 791
blood in, 796
chills in, 794
cholecystitis and, 792
diagnosis of, 797
from biliary intermittent fever, 798
from carcinoma, 837
from cholelithiasis, 798
from malarial fever, 798
dysentery and, 796
etiology of, 790
feces in, 796
fever in, 794
hepatic artery and, 791
veins and, 791
jaundice in, 794
leukocytosis in, 796
liver in, 795
lymphatics and, 792
multiple septicopyemic, 793
pain in, 794
pathology of, 792
portal vein and, 791
prognosis of, 798
rupture of, 796
subphrenic abscess and, 939
sweating in, 794
symptoms of, 792
traumatic, 792
treatment of, 798
tropical, 793
urine in, 795
in acute hepatitis, 789
acute yellow atrophy of, 767
alcoholism and, 768
bacillus coli and, 768
blood in, 771
chemistry of, 768
chloroform poisoning and, 768
diagnosis of, 771
from biliary cirrhosis, 772
from phosphorus poisoning, 772

Liver, acute yellow atrophy of, diarrhœa in, 771
etiology of, 767
fever in, 771
hemorrhages in, 771
jaundice in, 770
liver in, 771
pain in, 770
pathogenesis of, 770
pathology of, 768
phosphorus poisoning and, 768
pregnancy and, 768
prognosis of, 772
puerperal eclampsia and, 768
pulse in, 771
septicopyemia and, 768
spleen in, 771
symptoms of, 770
syphilis and, 768
treatment of, 772
urine in, 771
vomiting in, 771
amyloid, 763
anemia in, 764
ascites and, 897
diagnosis of, 764
from fatty liver, 763
diarrhœa in, 764
etiology of, 763
pathology of, 763
prognosis of, 764
spleen in, 764
symptoms of, 764
treatment of, 764
angioma of, 838
anomalies of, acquired, 751
congenital, 751
anthracosis of, 764
atrophy of, 760
general, 760
localized, 760
pathology of, 761
symptoms of, 761
bile pigments of, 717
salts of, 717
blood sugar and, 720
carbohydrate metabolism and, 720
carcinoma of, 833
ascites and, 834
diagnosis of, 835
from biliary cirrhosis, 836
from carcinoma of gall-bladder, 892
of stomach, 427
from hydatid disease, 837
from portal cirrhosis, 836
from syphilis of liver, 837
etiology of, 833
hydronephrosis in, 835
jaundice in, 834
liver in, 835
lungs in, 835
onset of, 833
pain in, 834
Liver, carcinoma of, pathology of, 833
primary, 833
prognosis of, 837
secondary, 833
spleen in, 835
symptoms of, 833
treatment of, 837
vomiting in, 835
cardiac, 777
in catarrhal cholangitis, 846
cholelithiasis and, 864
in chronic perihepatitis, 784
peritonitis, 957
cirrhosis of, 799
arthracotic, 822
ascites in, 815
epigastric murmur in, 816
fluids in, 816, 820
operation in, 825
tapping in, 815, 825
biliary, 826
alcohol and, 826
blood in, 829
diagnosis of, 830
from portal cirrhosis, 818, 830
dyspepsia in, 828
etiology of, 826
fever in, 829
hippocratic fingers in, 829
jaundice in, 828
liver in, 827
onset of, 828
pain in, 828
pathology of, 827
prognosis of, 831
spleen in, 828, 829
symptoms of, 828
treatment of, 831
urine in, 829
vomiting in, 828
breath in, 250
Budd's non-alcoholic, 802
in children, 822
circulation in, 805
diabetes mellitus and, 129
diagnosis of, from fatty liver, 763
from passive congestion, 779
from perihepatitis, 787
from tuberculous peritonitis, 965
dyspeptic, 802
experimental, 803
gall-bladder in, 806
Hanot's, 799, 826
hemochromatosis and, 820
hyperplasia in, 808
Laennec's, 799
malarial, 821
multilobular, 809
portal, 801
abdomen in, 814
albuminuria in, 810
alcohol and, 801
ascites in, 815
treatment of, 825
bile-ducts in, 808

Liver, cirrhosis of, portal, bilharzia hematobia in, 802
blood in, 817
bloodvessels in, 805
complications of, 817
constipation in, 812
diagnosis of, 818
ascitic fluid in, 820
from Banti's disease, 819
from biliary cirrhosis, 818, 830
from carcinoma of stomach, 819
from duodenal ulcer, 818
from gastric ulcer, 819
from portal thrombosis, 819
from splenic anemia, 819
from tuberculosis of peritoneum, 819
from tumors of peritoneum, 819
diarrhœa in, 812
etiology of, 801
fatty acids and, 802
fever in, 812
gastro-intestinal tract in, 809
heart in, 810
hematemesis in, 812
treatment of, 824
hemorrhages in, 813
hyperplasia in, 808
infections and, 802
jaundice in, 813
kidneys in, 810
liver in, 803, 814
lungs in, 810
malarial fever and, 802
nausea in, 812
nephritis in, 817
neuritis in, 818
œdema in, 816
pain in, 812
pathogenesis of, 811
pancreas in, 810
pathology of, 803
peritoneum in, 810
pleuritis in, 817
pneumonokoniosis and, 803
prognosis of, 822
signs in, 814
spleen in, 809, 815
symptoms of, 812
syphilis and, 802
stomach in, 810
tapping in, 815
toxemia in, 814
treatment of, 822
surgical, 825
tuberculosis and, 810, 817
types of, 820
typhoid fever and, 802
uncinaria duodenalis and, 802
Liver, cirrhosis of, portal, urine in, 817
vomiting in, 812
tuberculosis of peritoneum and, 817, 960
varieties of, 799
cloudy swelling of, 761
congestion of, 773
active, 773
diagnosis of, 775
etiology of, 773
jaundice in, 774
pain in, 774
pathology of, 774
prognosis of, 775
symptoms of, 774
treatment of, 775
vomiting in, 774
passive, 776
ascites in, 778
diagnosis of, 779
from cirrhosis, 779
from fatty liver, 763
etiology of, 776
heart in, 777
jaundice in, 778
œdema in, 778
pain in, 778
pathology of, 776
prognosis of, 779
symptoms of, 778
treatment of, 779
urine in, 778
constricted, 751
corset, 751
cysts of, 838
echinococcus, diagnosis of, from cysts of pancreas, 706
hydatid, subphrenic pyopneumothorax and, 949
deformities of, 751
in diabetes mellitus, 129, 138
diseases of, 715
acute peritonitis and, 911
disorders of, retrogressive, 760
displacement of, diagnosis of, from fatty liver, 763
incidence of, 991
effect of jaundice in, 740
emphysematous, 761
fatty, 761
alcohol and, 762, 763
diagnosis of, 763
from amyloid liver, 763
from cirrhosis of liver, 763
from displacement, 763
from leukemia, 763
from passive congestion, 763
etiology of, 762
metabolism and, 762
pathology of, 762
poisoning and, 762
prognosis of, 763
symptoms of, 763
treatment of, 763
tuberculosis and, 762, 763
vomiting in, 763
functions of, 715

Liver, functions of, bactericidal, 724
bile secreting, 716
detoxyfying, 722
disorders of, 715
glycogenic, 719
in iron metabolism, 725
lipogenic, 725
tests of, 726
Bernheim's test, 728
bromsulphalein, 728
dye, 728
Jones' test, 729
Rosenthal and White's test, 728
Sachs-Strauss levulose test, 729
van den Bergh test, 726
Widal's test, 731
urea-forming, 721
gaseous, 761
bacillus aërogenes capsulatus and, 761
hobnail, 804
hydatid disease of, diagnosis of, from carcinoma, 837
in jaundice, 740
leukemic enlargement of, diagnosis of, from fatty liver, 763
infiltration of, 766
malignant disease of, diagnosis of, from hepatitis, 787
necrosis of, acute, 767
in obesity, 211
parenchymatous degeneration of, 761
pericardiac pseudocirrhosis of, 783, 896
in pernicious anemia, 765
pigmentation of, 764
in anthracosis, 764
bilirubin in, 765
biliverdin in, 765
in hemochromatosis, 765
hemofuscin in, 766
hemosiderin in, 766
in malarial fevers, 765
red atrophy in, 765
silicosis in, 764
Riedel's lobe of, 752
sarcoma of, 837
sugar-iced, 783
in suppurative cholangitis, 851
syphilis of, ascites and, 897
chronic peritonitis and, 897
diagnosis of, from carcinoma, 837
from perihepatitis, 787
in thrombosis of portal vein, 757
tuberculosis of peritoneum and, 964
tumors of, benign, 838
malignant, 833
Wilson's disease and, 831
cirrhosis in, 832
liver in, 832
Loculated tuberculosis of peritoneum, 962
Ludwig's angina, 282
Lung, abscess of, breath in, 250
in carcinoma of liver, 835
in cirrhosis of liver, 810
Lung, gangrene of, breath in, 250
in obesity, 211
Lupus erythematosus of mouth, 261
Lymphangioma of intestines, 640
Lymphatic circulation, biliary infection and, 844
Lymphatics, abscess of liver and, 792
in biliary tract infection, 744
in carcinoma of stomach, 414
in cirrhosis of stomach, 481
Lymphocarcoma of intestines, 638
Lymphoid tissue, appendicitis and, 569

M

McBurney's point in appendicitis, 575
McKesson metabolor, 27
Macrochelia, 268
Macroglossia, 268
Malarial fevers, acute hepatitis and, 788
cirrhosis of liver and, 802, 821
diagnosis of, from abscess of liver, 798
from acute peritonitis, 927
from appendicitis, 586
from suppurative cholangitis 851
pigmentation of liver and, 765
Malnutrition, digestion and, 243
Maltose, metabolism of, 44
Measles, mouth in, 264
Mechanism of intestinal processes, automatic, 501
Meckel's diverticulum, intestinal obstruction from, 610
Medullary carcinoma of stomach, 412
Melanoglossia, 269
Melanotrichia of tongue, 269
Membranous cholecystitis, 856
colitis, 644
Meningitis, tuberculous, diabetes insipidus and, 172
Mental activity, metabolism in, 104
Mercurial stomatitis, 256
Merycism, 338
diagnosis of, 339
etiology of, 339
prognosis of, 339
symptoms of, 339
treatment of, 339
Mesenteric cysts of peritoneum, 974
glands, diseases of, acute peritonitis and, 911
embolism, 641
abdomen in, 643
diagnosis of, 643
diarrhœa in, 642
etiology of, 641
hemorrhage in, 642
pain in, 642
pathology of, 642
prognosis of, 643
symptoms of, 642
treatment of, 643
vomiting in, 642
thrombosis, 641

Mesenteric thrombosis, abdomen in, 643
arterial, 641
diagnosis of, 643
diarrhœa in, 642
etiology of, 641
hemorrhage in, 642
pain in, 642
pathology of, 642
prognosis of, 643
symptoms of, 642
treatment of, 643
venous, 641
vomiting in, 642
Mesentery, cyst of, diagnosis of, from cyst of pancreas, 707
suppuration in, 934
Meso-appendix, 565
Metabolic function of pancreas, impairment of, 662
Metabolism of acids, 70
in acromegaly, 128
of alcohol, 64
of alkalies, 70
amino-acids and, 29
basal, 28
in diabetes mellitus, 101
during growth, 91
effects of muscular exercise on, 84
in health, 73
mental activity and, 104
respiration and, 106
standards of, 74, 79
of blood, 65
of blood-sugar, 46
body temperature and, 93
of calcium, 69
in sprue, 651
of carbohydrates, 42
adrenals in, 127
in diabetes mellitus, 130, 131, 135
epinephrine in, 127
hypophysis in, 128
normal, 131
pancreas and, 662
parathyroid and, 129
in sympathicotonia, 127
thyroid and, 129
in vagotonia, 127
of cellulose, 45
cholelithiasis and, 866
of chlorine, 69
in diabetes mellitus, 101, 134
of disaccharides, 44
diseases of thyroid gland and, 102
dog experiments in, 30
epinephrine and, 103
fasting and, 31
of fat, 47
in diabetes mellitus, 132, 135
fatty liver and, 762
fever and, 100
foods and, 29
of foodstuffs, 37
of glycerol, 49
of glycogen, 44
in gout, 180
in hyperthyroidism, 102
Metabolism, incomplete proteins and, 29
in infants, observations on, 30
of iodine, 70
of iron, 69
function of liver in, 725
of ketones, 50
of lactose, 44
of lipins, 48
of maltose, 44
in mental activity, 104
methods of investigation of, 20
mineral, 68
of monosaccharides, 42
muscular work and, 28
in myxœdema, 102
in obesity, 102
of phospholipins, 49
of phosphorus, 69
of polysaccharides, 44
proportion of foodstuffs in, 37
of proteins, 52
in diabetes mellitus, 131, 135
in disease, 61
creatine in, 62
enzymes in, 183
hippuric acid in, 63
products of, 62
purines in, 63
specific dynamic action of food and, 84
urea in, 62
respiration apparatus in, 22, 24
results of, interpretation of, 30
starvation and, 32
thyroxin and, 102
in typhoid fever, 101
of uric acid in gout, 181
vitamines and, 29, 86
water balance in, 65
drinking at meals and, 68
intake in, 66
output in, 66
starvation and, 31
zones of, 41
Metastasis in carcinoma of intestines, 633
Meteorism, cause of, 509
in hepatoptosis, 996
in obstruction of intestine, 604
in peritonitis, 919
Micrococcus catarrhalis in mouth, 246
Microglossia, 268
Migraine in gout, 196
Mikulicz's disease, 281
Miliary aneurisms, hematemesis from, 488
Milky ascites, 900
Moeller's glossitis, 271
Monasaccharides, metabolism of, 42
Monilia enterica in sprue, 650
fecalis in sprue, 650
insolita in sprue, 650
intestinalis in sprue, 650
psilosis in sprue, 650
Morning diarrhœa, 533
in sprue, 653
Motor functions of intestines, 495
insufficiency of stomach, 456. *See* Stomach, dilatation of.

Motor paralysis of intestines, obstruction from, 625
Mouth, acne of, 262
actinomyces bovis in, 266
actinomycosis of, 266
anesthesia of, 250
angioneurotic œdema of, 261
bacillus gingivitidis in, 263
bacteriology of, 245
carcinoma of, 260
cysts of, 260
dermoid, 260
dermatoses of, 260
in diabetes mellitus, 263
diseases of, 245
disturbed sensation in, 250
dry, 276
eczema of, 262
erysipelas of, 262
in foot and mouth disease, 263
hyperesthesia of, 251
infection of, 246
inflammation of, 253
leprosy of, 267
in leukemia, 263
lichen planus of, 261
lupus erythematosis of, 261
in measles, 264
micrococcus catarrhalis in, 246
paresthesia of, 251
in pellagra, 263
pemphigus of, 261
treatment of, 262
in pernicious anemia, 263
in pregnancy, 264
psoriasis of, 261
sarcoma of, 260
in scarlet fever, 264
scleroderma of, 262
scleroma of, 267
in scurvy, 263
sepsis of, 246
in sprue, 263, 650
syphilis of, 265
primary sore in, 265
secondary lesions in, 266
tertiary lesions in, 266
treatment of 267
in tabes dorsalis, 264
tinea circinata of, 262
trench, 263
treponema pallidium in, 266
tuberculosis of, 264
diagnosis of, 265
treatment of, 265
tumors of, 260
mixed, 260
in typhoid fever, 262
in uremia, 262
urticaria of, 260
treatment of, 261
in varicella, 264
Movable kidney, diagnosis of, from appendicitis, 588
Movements of intestines, mechanism of, 496
Mucocele of appendix, 593
Mucofibrinous stomatitis, 254
Mucosal movements of intestines, 497
Mucous colic, 644
colitis, 239, 644
diarrhœa, 644
gastritis, 445
membrane in jaundice, 738
of stomach, atrophy of, diagnosis of, from carcinoma, 425
in dilatation, 463
Mucus hypersecretion in stomach, 330
Multiple sclerosis, diabetes mellitus and, 121
Multilobular cirrhosis of liver, 809
Muscles, abdominal, constipation and, 525
in peritonitis, 918
Muscular work and metabolism, 28
Myasthenia gravis, paralysis of œsophagus and, 290
Mycotic gastritis, 442
stomatitis, 258
Myocarditis in gout, 197
Myxœdema, metabolism in, 102
Myxoma of appendix, 593
of intestines, 640
of peritoneum, 969, 972
Myxomatous carcinoma of stomach, 413

N

Nausea in acute cholecystitis, 857
gastritis, 436
perihepatitis, 781
in appendicitis, 576
in carcinoma of pancreas, 711
in catarrhal cholangitis, 846
in cholera nostras, 541
in chronic gastritis, 450
in constipation, 525
in gall-stone colic, 871
in intestinal colic, 515
indigestion, 512
in mesenteric embolism, 642
in necrosis of pancreas, 676
in nephroptosis, 995
nervous, 346
in phlegmonous gastritis, 440
Necrosis of appendix, 571
fat, of pancreas, 665
hemorrhagic, of pancreas, 668
of liver, 767
of pancreas, diagnosis of, from suppurative pancreatitis, 679
Neoplasm, cholelithiasis and, 880
Nephritic colic, diagnosis of, from nervous gastralgia, 336
Nephritis, chronic, perihepatitis and, 784
diagnosis of, from diabetes insipidus, 175
diarrhœa and, 533
interstitial, in gout, 198
in nephroptosis, 995
in portal cirrhosis of liver, 812, 817
Nephrolithiasis, diagnosis of, from appendicitis, 587
Nephroptosis, 994

Nephroptosis, age and, 990
albuminuria in, 995
diagnosis of, 997
Dietl's crises in, 995
dilatation of stomach and, 995
gastrectasia in, 995
nausea in, 995
nephritis in, 995
pain in, 995
pregnancy and, 990
symptoms of, 994
treatment of 1001
urine in, 995
vomiting in, 995
Nervous anorexia, 362
diarrhœa, treatment of, 538
dyspepsia, 367
diagnosis of, from atony, 366
from dilatation, 466
eructation, 341
diagnosis of, 342
etiology of, 341
symptoms of, 342
treatment of, 342
gastralgia, 335
influences, diarrhœa and, 533
manifestations in gout, 196
mechanism of intestines, 496
nausea, 346
subacidity, 356
system in diabetes mellitus, 120, 139, 148
gastric atony and, 456
ulcer and, 376
in jaundice, 741
in motor insufficiency of stomach, 464
theory of gout, 189
vomiting, 342, 344
Neuralgia in gout, 196
intercostal, diagnosis of, from nervous gastralgia, 336
of intestines, 573, 575
ovarian, diagnosis of, from appendicitis, 588
Neurasthenia, achylia gastrica and, 358
cardiospasm and, 348
in constipation, 524
gastrica, 367
mucous colitis and, 646
nervous anorexia and, 362
dyspepsia and, 368
in splanchnoptosis, 992, 993
Neuritis, alcoholic, in cirrhosis of liver, 818
in diabetes mellitus, 148
treatment of, 168
Neurological changes in sprue, 654
Neuroma, gangliated, of peritoneum, 970
Neuropathic hematemesis, 488
Neuroses, gastric, 307
diagnosis of, from chronic gastritis, 453
polysymptomatic, 367
Nitrogen ammonia, 64
partition, 64
in urine in diabetes mellitus, 144
Noma, 256
Non-fatty ascites, 900
Novasurol in ascites, 907
Nuclein bases, 181
Nutrition in carcinoma of stomach, 417
in chronic gastritis, 450
in jaundice, 742
in mucous colitis, 646

O

Obesity, 209
age and, 209
alcohol and, 211
anemia, 213
appetite in, 214
blood in, 213
circumscribed, 216
complications of, 215
definition of, 209
diabetes mellitus and, 118, 119
diagnosis of, 216
from adiposis dolorosa, 216
from dystrophia adiposo-genitalis, 216
gland deficiency in, 216
endocrine disturbances in, 215
glands and, 209, 210, 215, 216, 221
enforced rest and, 210
etiology of, 209
gonad, 215
heart in, 211
heredity and, 209
in infants, 209
internal secretions and, 209, 210, 215, 216, 221
juvenile, treatment of, 222
kidneys in, 211
liver in, 211
localized, 216
treatment of, 222
lungs in, 211
metabolism in, 102
occupation and, 210
pathogenesis of, 211
pathology of, 211
physical signs in, 213
pituitary, 215
plethoric, 213
prognosis of, 216
sequelæ of, 215
sex and, 210
skin in, 214
stomach in, 211
symptoms of, 212
temperament and, 210
thyroid, 215
hyposecretion and, 210
treatment of, 217
dietetic, 217
mechanical, 220
medicinal, 221
prophylactic, 217
veins in, 211
Obliterating endophlebitis of hepatic veins, 755

Obliterative tuberculosis of peritoneum, 964
Obstipation, 519
Obstruction of intestines, 600
Obturation of intestines, 600
Occlusion of intestines, 600
"Occult blood" in carcinoma of stomach, 416
in gastric ulcer, 384
tests for, 384, 385
Œdema, angioneurotic, of mouth, 261
of œsophagus, 289
in chronic perihepatitis, 786
peritonitis, 958
in cirrhosis of liver, 816
in congestion of liver, 778
invisible, 67
salt-poor diet and, 76, 69
Œsophagitis, acute, 285
diagnosis of, 286
etiology of, 285
household lye and, 285
pathology of, 285
prognosis of, 286
sequelæ of, 286
symptoms of, 286
chronic, 286
symptoms of, 286
treatment of, 287
traumatic, 285
treatment of, 286
Œophagoscopy in diagnosis of diseases of œsophagus, 284
for foreign bodies in œsophagus, 306
Œsophagus, actinomycosis of, 289
anginoneurotic œdema of, 289
carcinoma of, 300
cough in, 301
diagnosis of, 301
from cardiospasm, 350
from hematemesis, 487
etiology of, 300
pathology of, 301
prognosis of, 302
symptoms of, 301
treatment of, 302
congenital diverticulum of, 285
malformations of, treatment of, 285
stricture of, 285
webs of, 285
description of, 283
dilatation of, 290
cardiospasm and, 347
diagnosis of, 291
from dilatation of stomach, 466
diffuse, 290
idiopathic, 291
treatment of, 291
diseases of, 283
diagnosis of, 283
history in, 284
œsophagoscopy in, 284
roentgen-ray examination in, 283
diverticulum of, 293
Œsophagus, diverticulum of, breath in, 250
diagnosis of, 295
etiology of, 294
pathology of, 294
prognosis of, 296
pulse in, 294
symptoms of, 295
traction, 294
treatment of, 296
foreign bodies in, 303
diagnosis of, 304
dysphagia in, 303
œsophagoscopy for, 306
contraindications to, 306
prognosis of, 305
prophylaxis in, 306
symptoms of, 303
treatment of 306
herpes of, 289
imperforate, 285
infective granuloma of, 288
inflammation of, 285
paralysis of, 289
diagnosis of, 290
etiology of, 290
myasthenia gravis and, 290
poliomyelitis and, 290
symptoms of, 290
syndrome of Avellis and, 290
syphilis and, 290
treatment of, 290
rupture of, 288
sarcoma of, 302
stenosis of, compression, 298
non-malignant, 297
spasmodic, 297
cricopharyngeal, 297
diagnosis of, 297
treatment of, 298
stricture of, cicatricial, 298
diagnosis of, 300
non-malignant, 297
prognosis of, 300
symptoms of, 299
treatment of, 300
syphilis of, 289
trauma of, 288
tuberculosis of, 288
tumors of, benign, 303
ulcers of, 287
diagnosis of, 287
with hematemesis, 487
prognosis of, 287
symptoms of, 287
treatment of, 287
varix of, 289
diagnosis of, with hematemesis, 487
Oïdium albicans, 258
in sprue, 650
Omental cysts of peritoneum, 976
Omentum, abscess of, 935
inflammation of, 934
tumors of, diagnosis of, from carcinoma of stomach, 427
volvulus of, 624

Omentum, volvulus of, symptoms of, 625
treatment of, 625
Oöphoritis, diagnosis of, from appendicitis, 588
Optic neuritis in diabetes mellitus, 149
Oral sepsis, 246
Ovarian cysts, acute peritonitis and, 911
diagnosis of, from ascites, 903
from cyst of pancreas, 907
neuralgia, diagnosis of, from appendicitis, 588
Oxyuris vermicularis, appendicitis and, 568

P

Pain in abscess of liver, 794
in achylia gastrica, 359
in acute cholecystitis, 857
enteritis, 540
gastritis, 436
hepatitis, 789
perihepatitis, 781
peritonitis, 918, 932
yellow atrophy of liver, 770
in aneurism of hepatic artery, 754
in appendicitis, 574
in calculus of pancreas, 695
in carcinoma of gall-bladder, 890
of liver, 834
of œsophagus, 301
of pancreas, 711
of stomach, 416
in cardiospasm, 349
in cholelithiasis, 871
in cholera nostras, 541
in chronic peritonitis, 954
in cirrhosis of liver, 812, 828
of stomach, 482
in colitis, 546
in congestion of liver, 774, 778
in constipation, 524
in cysts of pancreas, 705
in diarrhœa, 536
in dilatation of stomach, 460, 464
in duodenal ulcer, 406, 556
in gall-stone colic, 871
in gastric ulcer, 382
in hemoperitoneum, 908
in hepatoptosis, 996
in hyperacidity, 317
in idiopathic dilatation of colon, 537
in intestinal colic, 514
indigestion, 512
in intussusception, 618
in mesenteric embolism, 642
thrombosis, 642
in nephroptosis, 995
in nervous gastralgia, 335
in obstruction of intestines, 603
in pancreatitis, 675, 690
in perforation of gastric ulcer, 393
in phlegmonous gastritis, 440
in pylorospasm, 352
in splanchnoptosis, 992
in subphrenic abscess, 946
Pain in subphrenic pyopneumothorax, 950
in suppurative cholangitis, 850
pancreatitis, 683
in syphilis of stomach, 492
in tongue, 272
in toxic gastritis, 442
in tuberculosis of peritoneum, 963
in ulcer of intestines, 562
in volvulus, 620
Painful gastric emptiness, 334
Palate, soft, paralysis of, 270
tuberculosis of, 265
Pancreas, abscess of, calculus and, 695
subphrenic abscess and, 939
acute dilatation of stomach and, 460
adenoma of, 710
alimentary glycosuria and, 664
calculi of, 693
abscess of pancreas in, 695
azotorrhœa in, 696
carcinoma of pancreas and, 696
colic in, 695
complications of, 696
diabetes mellitus in, 122, 695
diagnosis of, 696
from biliary colic, 697
etiology of, 693
glycosuria in, 696
jaundice in, 695
loss of weight in, 696
pain in, 695
pathology of, 693
steatorrhœa in, 696
symptoms of, 695
treatment of, 697
carbohydrate metabolism and, 662
carcinoma of, 709
ascites in, 712
cachexia in, 713
calculus of pancreas and, 696
constipation in, 711
diabetes mellitus in, 122, 710, 712
diagnosis of, 713
from cholelithiasis, 713
diarrhœa in, 711
duration of, 713
fatty stools in, 711
fever in, 713
gall-bladder in, 712
glycosuria in, 712
incidence of, 709
jaundice in, 712
liver in, 712,
nausea in, 711
pain in, 711
pathology of, 709
secondary, 709
symptoms of, 711
treatment of, 714
tumor of, 710, 711
vomiting in, 711
in cirrhosis of liver, 810
cyst of, 698
ascites in, 705
classification of, 698
congenital, 701
contents of, 703

Pancreas, cyst of, diabetes mellitus in, 122, 706
diagnosis of, 706
from aortic aneurism, 707
from cysts of mesentery, 707
from echinococcus cysts of liver, 706
from hydronephrosis, 707
from ovarian cysts, 707
etiology of, 701
functional disturbance in, 705
hydatid, 701
jaundice in, 705
loss of weight in, 706
necrosis of pancreas and, 679
pain in, 705
pathology of, 701
position of, 699
proliferation, 702
pseudocysts, 698
retention, 701
steatorrhœa in, 705
symptoms of, 703
traumatic, 701
treatment of, 707
true, 698
tumor in, 703
disappearance of, 704
movable, 704
relation of, to adjacent organs, 704
descent of, 997
in diabetes mellitus, 122, 123, 124, 622 710
diseases of, 657
azotorrhœa in, 660
in children, development of, 664
diagnosis of, from carcinoma of stomach
feces in, 659
glycosuria and, 661
metabolic function and, 662
pancreatic secretion and, 657
pathology of, 657
steatorrhœa in, 658
symptoms of, 657
displaced, 997
gangrene of, 672, 674
hydropic degeneration of, 124
infantilism and, 664
necrosis of, fat, 665
bacillus coli in, 665
clinical significance of, 667
etiology of, 665
experimental, 665
pathology of, 666
urine in, 668
hemorrhagic, 668
ascaria lumbricoides in, 672
bacteria and, 670
cholelithiasis and, 670
complications of, 678
constipation in, 676
cysts of pancreas in, 679
diagnosis of, 679
from biliary colic, 679
Pancreas, necrosis of, hemorrhagic, diagnosis of, from perforation of gall-bladder, 679
from ruptured aneurism, 680
from suppurative pancreatitis, 679
duodenitis and, 672
etiology of, 670
feces in, 676
fever in, 676
gangrene in, feces in, 678
fever in, 677
glycosuria in, 678
jaundice in, 678
leukocytosis in, 677
tumor in, 677
glycosuria in, 676
jaundice in, 676
leukocytosis in, 676
nausea in, 676
necrotic stage of, 675
onset of, 675
operation in, 681
pain in, 675
pathology of, 673
sequelæ of, 678
shock in, 676
symptoms of, 674
traumatic, 672
treatment of, 680
tumor in, 676
urine in, 676
vomiting in, 676
sarcoma of, 710
secretion of, fat absorption and, 659
syphilis of, 692
diabetes mellitus and, 124
tuberculosis of, 692
tumors of, dilatation of stomach and, 462
Pancreatic apoplexy, 669
colic in calculi of pancreas, 695
cysts, 679
enzymes in duodenal contents, 657
juice, ferments of, 498
secretion of, 498
sialorrhœa, 241
Pancreatitis, 241, 665
acute diagnosis of, from acute peritonitis, 926
from appendicitis, 586
from duodenal ulcer, 558
cholelithiasis and, 670, 877
chronic, 686
diagnosis of, 691
interacinar, 689
interlobular, 689
interstitial, 123, 686
alcoholism and, 688
arteriosclerosis and, 688
cholelithiasis and, 691
diabetes mellitus and, 122, 691
etiology of, 686

Pancreatitis, chronic interstitial, glycosuria in, 691
hemochromatosis and, 690
pain in, 690
pathology of, 688
symptoms of, 690
vomiting in, 690
diabetes mellitus and, 122, 691
experimental, 665
gall-stones and, 681, 686
hemorrhagic, ascaris and, 672
bile and, 671
diabetes mellitus and, 122
suppurative, 681
bacteriology of, 682
constipation in, 683
diagnosis of, 685
from hemorrhagic necrosis, 679
diarrhœa in, 683
emaciation in, 684
etiology of, 682
fever in, 683
glycosuria in, 684
jaundice in, 683
leukocytosis in, 684
onset of, 683
pain in, 683
pathology of, 682
peritonitis in, 684
sequelæ of, 684
symptoms of, 683
treatment of, 685
tumor in, 684
vomiting in, 683
Papillitis lingualis, 271
Paracentesis abdominis in ascites, 906
Paragusia, 251
Paralysis of intestines, obstruction from, 625
of œsophagus, 289
of soft palate, 270
of tongue, 269
Paraplegia in diabetes mellitus, 148
Parasites, appendicitis and, 568
Parasitic cysts of peritoneum, 972
Parathyroid glands, carbohydrate metabolism and, 129
diabetes mellitus and, 129
Parenchymatous degeneration of liver, 761
hepatitis, 788
Paresis in diabetes mellitus, 121, 148
Paresthesia of mouth, 251
Paronychia in diabetes mellitus, 146
Parorexia, 334
Parotid gland, inflammation of, 277
mixed tumor of, 279
Parotitis, acute, 277
chronic, 277
gastric ulcer and, 395
in subphrenic pyopneumothorax, 951
Pellagra, diagnosis of, from sprue, 654
mouth in, 263
vitamines and, 91
Pelvic infections, cholelithiasis and, 865
Pentosuria, 154
Pepsin, secretion of, in gastritis, 451
Peptic ulcer, 371
structure and function in relation to, 232
Perforating ulcer of foot in diabetes mellitus, 146
of stomach, 371
Perforation in duodenal ulcer, 557
of intestines, carcinoma and, 633
Peri-appendicular abscess, 572
rupture of, 572
Pericarditic pseudocirrhosis of liver, 783, 896
Pericarditis, chronic perihepatitis and, 784
peritonitis and, 954
in gout, 198
Pericholecystic adhesions, cholelithiasis and, 877
Pericolic abscesses, 936
diagnosis of, 936
subphrenic abscess and, 939
symptoms of, 936
treatment of, 936
Pericolitis, 563, 933
diagnosis of, 564
etiology of, 563, 933
pathology of, 563
sinistra, 564, 933
symptoms of, 564, 933
treatment of, 564, 933
Perigastric abscess, 935
adhesions in stenosis of pylorus, 467
Perigastritis, diagnosis of, from carcinoma of stomach, 426
dilatation of stomach and, 462
in gastric ulcer, 391
Perihepatitis, 780
acute, 780
ascites in, 781
diagnosis of, 781
etiology of, 780
hiccough in, 781
nausea in, 781
pain in, 781
pathology of, 781
prognosis of, 782
symptoms of, 781
treatment of, 782
vomiting in, 781
chronic, general, 783
abdomen in, 785
ascites in, 786
chronic nephritis and, 784
diagnosis of, 786
from cirrhosis, 787
from malignant disease, 787
from syphilis, 787
from tuberculous peritonitis, 787
etiology of, 783
infections and, 784
liver in, 784
œdema in, 786
pathology of, 783
pericarditis in, 784
pleuritis in, 786
prognosis of, 787

Perihepatitis, chronic, general, spleen in, 784
symptoms of, 785
syphilis and, 783
treatment of, 787
urine in, 786
hyperplastic, 783
local, 782
deforming, 783
hyaline, 783
Perimesosigmoiditis, 953
Periodical vomiting, 344
in children, 345
Perisigmoiditis, 933
Peristalsis in cirrhosis of stomach, 482
in congenital hypertrophic stenosis of pylorus, 475
in intestinal colic, 514
of intestines, 495
increased, 496
pathological, 496
tonic, 497
Peristaltic unrest, 355
Peritoneal sanguineous cysts, 976
Peritoneum, adhesions of, 957
comparison of, with other serous membranes, 895
cysts of, 972
conditions simulating, 979
cysticercus cellulosæ, 974
embryonic, 977
hydatid, 972
clinical aspects of, 973
diagnosis of, 973
pathology of, 972
treatment of, 974
mesenteric, 974
diagnosis of, 975
pathogeny of, 974
pathology of, 975
signs of, 975
symptoms of, 975
treatment of, 975
omental, 976
diagnosis of, 976
symptoms of, 976
retroperitoneal, 978
sanguineous, 976
diagnosis of, 977
morbid anatomy of, 976
symptoms of, 977
treatment of, 977
tænia echinococcus in, 972
urachal, 978
diseases of, 894
hemorrhage into, diagnosis of, from acute peritonitis, 926
fibroma of, 969
fibromyoma of, 969
gangliated neuroma of, 970
immunity of, 896
lipoma of, 970
lymphatics of, 895
myoma of, 969
myxoma of, 972
pain from, 895
pseudomyxoma of, 979
Peritoneum, retroperitoneal hematoma of, 977
tuberculosis of, 959
abdomen in, 963
adhesive, 962
age and, 959
alcoholism and, 960
ascitic, 963
bacteriology of, 960
blood in, 964
chronic fibroid, 962
cirrhosis of liver and, 960
complications of, 965
diagnosis of, 965
from tumor, 966
from typhoid fever, 965
encysted, 962, 963
etiology of, 959
feces in, 964
fever in, 964
jaundice in, 965
leukocytosis in, 964
liver in, 964
loculated, 962
obliterative, 964
onset of, 963
pain in, 963
pathology of, 961
paths of infection in, 960
pregnancy and, 960
prognosis of, 966
sex and, 960
spleen in, 964
suppurative, 963
symptoms of, 963
treatment of, 967
heliotherapy in, 967
hygienic, 968
medical, 967
surgical, 968
vaccine, 967
ulcerative, 963
tumors of, 968
diagnosis of, from tuberculosis, 966
malignant, 979
primary, 979
diagnosis of, 982
etiology of, 981
pathology of, 979
treatment of, 982
secondary, 982
diagnosis of, 984
pathology of, 982
prognosis of, 985
symptoms of, 983
treatment of, 985
non-malignant, 969
urine in, 964
Peritonitis, acute circumscribed, 932
non-suppurative, 932
pain in, 932
symptoms of, 932
treatment of, 933
diffuse, 909
abdomen in, 918
abscess and, 911

Peritonitis, acute diffuse, age and, 912
bacillus aërogenes capsulatus in, 913
coli in, 912
pyocyaneus in, 912
typhosus in, 913
bacteriology of, 912
blood in, 922
cultures in, 922
collapse in, 916
constipation in, 920
cytology in, 915
diagnosis of, 925
age in, 927
from Addison's disease, 927
from hemorrhage into peritoneum, 926
from intestinal obstruction, 926
from malaria, 927
from pancreatitis, 926
from pneumonia, 926
from pleurisy, 927
from tympanites, 926
from uremia, 927
history in, 928
sex in, 927
diseases of appendix and, 911
of colon and, 911
of gall-bladder and, 911
of intestines and, 911
of liver and, 911
of mesenteric glands and, 911
of spleen and, 911
of stomach and, 911
distention in, 919
duration of, 922
etiology of, 910
facies in, 917
fever in, 921
hiccough in, 920
onset of, 917
ovarian cysts and, 911
pain in, 918
pathogeny of, 909
pathology of, 913
percussion in, 919
perforation of uterus and, 911
position in, 917
primary, 910
prognosis of, 928
pulse in, 921
pyosalpinx and, 911
respiration in, 920
rigors in, 920
secondary ,910
sex and, 912
staphylococci in, 912, 913
streptococcus in, 913
symptoms of, 916
tenderness in, 918
thirst in, 917
treatment of, 929
medical, 931
prophylactic, 929
serum, 932
surgical, 929
transfusion in, 930
urine in, 922
vomiting in, 920
ascites and, 897
carcinoma of intestines and, 633
chronic diffuse, 954
abdomen in, 958
age in, 958
alcoholism and, 955
arteriosclerosis and, 955
ascites in, 958
bacillus coli in, 956
tuberculosis in, 956
typhosus in, 956
constipation in, 958
diagnosis of, 958
gall-bladder in, 957
granular kidney and, 955
liver in, 957
œdema in, 958
onset of, 958
pathology of, 956
pericarditis and, 954
pleuritis and, 954
prognosis of, 958
respiration in, 958
sex in, 958
spleen in, 957
symptoms of, 958
syphilis and, 955
treatment of, 959
tuberculosis and, 956
simple, adhesions in, 957
appendicitis and, 952
cholecystitis and, 953
constipation in, 953
duodenal ulcer and, 952
gastric ulcer and, 952
jaundice in, 953
localized, 952
bands from, 954
mesenteric, 953, 954
pain in, 954
puerperal infection and, 952
from intussusception, 617
malignant, 982
pneumococcic, 923
prognosis of, 924
symptoms of, 924
primary idiopathic, 910
progressive fibrinopurulent, 914
puerperal, 924
secondary, 910
in suppurative pancreatitis, 684
tuberculous, 959
forms of, 961
diagnosis of, from hepatic cirrhosis, 965
Perityphilitis, 564, 589
Pernicious anemia, diagnosis of, from sprue, 654
mouth in, 263
pigmentation of liver and, 765

Petechiæ in toxic gastritis, 442
Pettenkofer-Voit respiration chamber, 24
Phantom tumor, 510
Phlebitis in gout, 198
suppurative, of hepatic veins, 955
Phlegmonous cholecystitis, 856
gastritis, 438
Phloridzin diabetes, 130
Phospholipins, 48
Phosphorus, metabolism of, 69
poisoning, acute yellow atrophy of liver and, 768
diagnosis of, from acute yellow atrophy of liver, 772
Phrenospasm, 291
etiology of, 291
pathology of, 292
symptoms of, 292
diagnosis of, 293
prognosis of, 293
treatment of, 293
Pick's disease, 783
Pigmentation of liver, 764
Pituitary adiposity, 215
gland, diabetes insipidus and, 170
obesity, 215
tartrate, 173
Pituitrin in diabetes insipidus, 176
Plethoric obesity, 213
Pleural effusion, diagnosis of, from subphrenic abscess, 947
Pleuritis in cirrhosis of liver, 817
chronic perihepatitis and, 786
peritonitis and, 954
diagnosis of, from acute peritonitis, 927
in subphrenic pyopneumothorax, 951
Pneumatosis, 355
Pneumaturia in diabetes mellitus, 146
Pneumococcus, peritonitis from 923
Pneumonia in diabetes mellitus, 148
diagnosis of, from acute peritonitis, 926
from appendicitis, 586
Pneumonokoniosis, cirrhosis of liver and, 803
Poisoning, chloroform, acute yellow atrophy of liver and, 772
fatty liver and, 762
lead, gout and, 180
phosphorus, acute yellow atrophy of liver and, 772
Poliomyelitis, paralysis of œsophagus and, 290
Polydipsia in diabetes mellitus, 140
Polyorrhomenitis, 783
Polyphagia in diabetes mellitus, 140
diagnosis of, from acoria, 361
from bulimia, 333
Polyps of appendix, 593
Polysaccharides, metabolism of, 44
Polysymptomatic neuroses, 367
Polyuria in diabetes insipidus, 174
mellitus, 140
Portal circulation, biliary infections through, 843
cirrhosis of liver, 758, 801
Portal cirrhosis of liver, diagnosis of, from biliary cirrhosis, 818, 830
from carcinoma, 836
pyemia, 758
vein, abscess of liver and, 791
diseases of, 755
pylephlebitis adhesiva of, 755
pyelothrombosis of, 755
thrombosis of, 755
ascites in, 757, 898
diagnosis of, 757
from cirrhosis of liver, 819
diarrhœa in, 758
enlargement of spleen in, 758
etiology of, 756
hematemesis in, 758
intestinal hemorrhage in, 757
obstruction in, 758
intrahepatic, 756
liver in, 757
main trunk of, 756
pathology of, 756
peripheral vessels, 756
prognosis of, 758
symptoms of, 757
treatment of, 758
vomiting in, 757
Pregnancy, acute yellow atrophy of liver and, 768
cholelithiasis and, 865
diabetes mellitus and, 120
treatment of, 168
mouth in, 264
nephroptosis and, 990
splanchnoptosis and, 990
tuberculosis of peritoneum and, 960
Presbyopia in diabetes mellitus, 149
Preventiculosis, 291
Progressive lenticular degeneration, 831
Proliferation cysts of pancreas, 702
Prosecretin, 498
Prostration in intestinal obstruction, 606
Proteins, classification of, 53
daily consumption of, 56
digestion of, 53
incomplete, metabolism and, 29
metabolism of, 52
in diabetes, 62
in disease, 61
enzymes in, 183
in fasting, 34
in undernutrition, 61
minimum in diet, 57
products of, 62
ration, liberal, 60
optional, 58
Pruritus in catarrhal cholangitis, 846
in diabetes mellitus, 146
treatment of, 168
in jaundice, 739
Pseudocirrhosis, pericardial, 783, 896
Pseudomyxoma of peritoneum, 979
Psoriasis linguæ, 272
of mouth, 261
Psychic vomiting, 344

Psychoneuroses, digestion and, 225, 243
Ptyalism, 276
Puerperal eclampsia, acute yellow atrophy of liver and, 768
infections, cholelithiasis and, 865
chronic peritonitis and, 956
peritonitis, 924
Pulmonary embolism in subphrenic abscess, 946
Pulse in acute peritonitis, 921
in appendicitis, 577
Purin, 182
bodies, 182
in protein metabolism, 63
uric acid and, 185, 188
Pus in carcinoma of intestines, 637
of stomach, 416
Pyelitis, acute, diagnosis of, from appendicitis, 587
Pyemia, portal, 758
Pylephlebitis adhesiva of portal vein, 755
suppurative, 758
diagnosis of, 759
from suppurative cholangitis, 851
diarrhœa in, 759
hematemesis in, 759
pathology of, 759
prognosis of, 759
symptoms of, 759
treatment of, 760
vomiting in, 759
Pylethrombosis of portal vein, 755
Pyloric disease, 472
stenosis, hypertrophic, 230
Pylorospasm, 351, 466
acute dilatation and, 460
congenital, 472
hypertrophic stenosis of pylorus and, 472
diagnosis of, 353
etiology of, 352
gastrosuccorrhœa in, 353
pain in, 352
reflex, 353
symptoms of, 352
treatment of, 354
vagotonia and, 351
vomiting in, 352
Pylorus, chemical control of, 309
incontinence of, etiology of, 364
symptoms of, 364
treatment of, 364
nervous control of, 308
spasm of, diagnosis of, from carcinoma of stomach, 428
dilatation of stomach and, 462
stenosis of, 466
benign, 466
cicatricial, 466
foreign bodies and, 467
from carcinoma of stomach, 467
from external pressure, 467
gastric ulcer and, 395
hypertrophic, 467
congenital, 472
constipation in, 475
Pylorus, stenosis of, hypertrophic congenital, diagnosis of, 475
differential, 476
dilatation in, 475
hypertrophy and, 472
pathogenesis of, 472
pathology of, 472
peristalsis in, 475
prognosis of, 476
pylorospasm and, 472
signs in, 475
symptoms of, 474
treatment of, 476
atropine in, 477
surgical, 477
tumor in, 475
vomiting in, 475
diagnosis of, from carcinoma of stomach, 428
dilatation of stomach and, 462
impaction of food and, 677
varieties of, 466
ulcer of, diagnosis of, from carcinoma of stomach, 428
Pyopneumothorax, subphrenic, 948
Pyorrhœa alveolaris, 247
diagnosis of, 248
treatment of, 248
Pyosalpinx, acute peritonitis and, 911

R

Ranula, 260
pancreatica, 701
Rectum, syphilis of, 598
Redundancy of colon, 531
Reflexes in diabetes mellitus, 149
Reflex vomiting, 345
Regurgitation, gastric, 340. *See* Gastric regurgitation.
Relapsing appendicitis, 582
Renal colic, diagnosis of, from appendicitis, 587
diabetes, 130
dropsy, ascites and, 898
theory of gout, 189
Rennet ferment in chronic gastritis, 451
Residual peritoneal abscesses, 937
Respiration in acute peritonitis, 920
apparatus, 22, 24
closed circuit, 26
open circuit, 27
basal metabolism and, 106
in chronic peritonitis, 958
Respiratory coefficient in diabetes mellitus, 135
quotient in diabetes mellitus, 41
in fasting, 32
system in gout, 193
Retention cysts of pancreas, 701
Retinitis in diabetes mellitus, 149
Retrocedent gout, 197
Retrogressive disorders of liver, 760
Retroperitoneal abscesses, 937
[illegible]s of peritoneum, 978

Retroperitoneal hematoma of peritoneum, 977
sarcoma, 968
Rhythmic segmentation of intestines, 495
Rhythmicity in digestive tract, 309
Rickets, etiology of, 90
vitamines and, 90
Riedel's lobe of liver, 752
Riga's disease, 274
Rigors in acute peritonitis, 920
Roentgen-ray examination in diagnosis of carcinoma of stomach, 424
of diseases of œsophagus, 283
of gall-stones, 879
of gout, 199
in duodenal ulcer, 407
in gastric ulcer, 386
in redundancy of colon, 532
in syphilis of stomach, 493
findings in constipation, 523
Rosenthal and White's liver functional tests, 728
Round ulcer, 371
Rumination, 338. *See* Merycism.
Rupture of œsophagus, 288

S

Saccharomyces albicans buccalis, 258
Saccharose, 44
Sachs-Strauss levulose liver functional test, 729
Saliva, 275
chorda, 275
composition of, 275
in diabetes, 275
paralytic, 275
secretion of, 275
absence of, 276
diminution of, 276
increase of, 276
sympathetic, 275
Salivary calculi, 279
gland, atrophy of, 282
diseases of, 275
enlargement of, 281
stone in, 279
swelling of, 278
syphilis of, 278
tuberculosis of, 278
tumors of, 279
treatment of, 280
secretion, absence of, 276
diminution of, 276
increase of, 276
Salivation, 256, 276
in children, 276
mercurial, 256
Salpingitis, diagnosis of, from appendicitis, 588
Sand, intestinal, 504
in mucous colitis, 646
Sanguineous cysts of peritoneum, 976
Sarcinæ in carcinoma of stomach, 421
Sarcoma of appendix, 594
of intestines, 638
Sarcoma of liver, 837
of mouth, 260
of œsophagus, 302
of pancreas, 710
retroperitoneal, 980
of tongue, 274
Scarlet fever, mouth in, 264
Sciatica in gout, 196
Scirrhus carcinoma of stomach, 412
Scleroderma of mouth, 262
Scleroma of mouth, 267
Scrotal tongue, 269
Scurvy, etiology of, 90
mouth in, 263
vitamines and, 90
Secretin, 225, 498, 499
Secretion of saliva, 275
Sensation, oral, disturbances of, 250
Sepsis, oral, 246
Septicemia in appendicitis, 580
breath in, 250
Septicopyemia abscess of liver in, 793
acute yellow atrophy of liver and, 768
Serositis, multiple, 783
Serum test in carcinoma of stomach, 423
Shock in necrosis of pancreas, 676
Sialodochitis fibrinosa, 278
Sialorrhœa, 276
pancreatic, 241
Sialosis, 276
Silicosis, hepatic 764
Sitophobia, 363
Skin in acute catarrhal cholangitis, 846
in diabetes mellitus, 137, 146
in gout, 196
in jaundice, 738
in obesity, 214
Smoker's patch, 273
Sodium chloride in urine in diabetes mellitus, 145
phosphate in urine in diabetes mellitus, 145
sulphate in urine in diabetes mellitus, 145
urate crystals in gout, 199
Solomon's test in diagnosis of carcinoma of stomach, 423
Spasm of pylorus, diagnosis of, from carcinoma of stomach, 428
dilatation of stomach and, 462
of tongue, 269
Spasmodic stenosis of œsophagus, 297
Spastic constipation, 523
Spinal cord changes in sprue, 654
Spine, deformities of, acute dilatation of stomach and, 459
tuberculosis of, subphrenic abscess and, 940
Splanchnoptosis, 986
abdomen in, 992
age in, 990
cachectic, 993
congenital, 987
constipation in, 992
diagnosis of, 997
digestion and, 242
etiology of, 988

Splanchnoptosis, frequency of, 989
gastro-intestinal, 993
hepatic, 993
indigestion in, 992
lithemic, 993
movable kidney and, 989
neurasthenia in, 992, 993
pain in, 992
pathogenesis of, 987
pregnancy and, 990
prognosis of, 999
symptoms of, 991
treatment of, 999
vomiting in, 992
Spleen in acute hepatitis, 789
yellow atrophy of liver, 771
in amyloid liver, 764
in carcinoma of liver, 835
in catarrhal cholangitis, 846
in chronic perihepatitis, 784
peritonitis, 957
in cirrhosis of liver, 809, 815, 828, 829
descent of, 996
diagnosis of, 998
diseases of, acute peritonitis and, 911
enlargement of, in thrombosis of portal vein, 758
movable, 991
perforation of gastric ulcer into, 393
in tuberculosis of peritoneum, 964
Splenic anemia, diagnosis of, from cirrhosis of liver, 819
Splenomegalic hemolytic jaundice, 737
Splenoptosis, 996
Sprue, 649
Addisonian anemia and, 649, 654
anemia in, 649, 654
blood in, 654
transfusion in, 655
calcium metabolism in, 651
cord changes in, 654
diagnosis of, 654
from pellagra, 654
from pernicious anemia, 654
diarrhœa in, 653
etiology of, 650
loss of weight in, 654
monilia in, 650
mouth in, 263, 650
neurological changes in, 654
oïdium albicans in, 650
pathology of, 651
prognosis of, 654
stools in, 653
strongyloides stercoralis in, 649
symptoms of, 652
tongue in, 652, 655
Squamous-celled cancer of stomach, 413
Staphylococcus aureus in infections of biliary tract, 842
epidermidis albus in acute peritonitis, 912
pyogenes albus in acute peritonitis, 912
aureus in acute peritonitis, 913
Starvation, metabolism and, 32
water, 37
Steapsin, 499
Steatorrhœa in calculus of pancreas, 696
in cysts of pancreas, 705
in diseases of pancreas, 658
feces in, 659
Stenosing gastritis, 467
tuberculosis of intestines, 596
Stenosis, cardiac, gastric ulcers and, 395
of duodenum, 466
of intestine, congenital, obstruction from, 614
of œsophagus, compression, 298
non-malignant, 297
spasmodic, 297
of pylorus, 406
cicatricial, 466
congenital hypertrophic, 472
gastric ulcer and, 395
hypertrophic, diagnosis of, from carcinoma of stomach, 428
Stercoral ulcers of intestines, 561
Sterols, 48
Stomach, absence of mucus in, 332
anacidity of, 357. *See* Achylia gastrica.
atony of, 231, 364
appetite in, 365
breath in, 250
cholelithiasis and, 365
constipation in, 365
diagnosis of, 366
from hyperacidity, 320
from nervous dyspepsia, 366
enteroptosis in, 366
etiology of, 365
gastric contents in, 366
gastroptosis in, 366
hyperacidity and, 319
prognosis of, 366
symptoms of, 365
treatment of, 366
vertigo in, 366
carcinoma of, 409
abdominal examination in, 417
acetic acid in, 420
adenitis in, 419
adenocarcinomatous, 412
age in, 409
alcoholism and, 410
amœba in, 422
anemia in, 417
anorexia in, 415
auscultation in, 419
auto-inoculation and, 410
blood stream in, 414
Boas-Oppler bacillus in, 421
bowels in, 416
butyric acid in, 420
colloid, 412
constipation in, treatment of, 431
diagnosis of, 422
blood-sugar content in, 423
from achylia gastrica, 360
from atrophy, of mucous membrane, 425
from carcinoma of duodenum, 426

Stomach, carcinoma of, diagnosis of, from carcinoma of liver, 427
from chronic gastritis, 425, 453
from cirrhosis of liver, 819
from disease of pancreas, 427
from gastric ulcer, 390
from nervous dyspepsia, 369
gastralgia, 336
from perigastritis, 426
from spasm of pylorus, 428
from stenosis of pylorus, 428
from tuberculosis of peritoneum, 427
from tumors of colon, 427
of gall-bladder, 427
of omentum, 427
of peritoneum, 427
from ulcer of pylorus, 428
roentgen-rays in, 424
serum test in, 423
Solomon's test in, 423
of tumor, 422
diarrhœa in, treatment of, 431
digestive symptoms in, 415
dissemination of, 413
duration of, 429
etiology of, 409
extension of, 413
ferments in, 420
fever in, 417
flagellates in, 422
flatulence in, 415
functional signs in, 419
gastrectomy in, 432
gastric analysis in, 419
rigidity in, 418
ulcer and, 410
gastrostomy in, 434
hematemesis in, 416, 488
heredity in, 410
inflation in, 418
inspection in, 417
lactic acid in, 420
latent, 414
lymphatics in, 414
medullary, 412
metastases in, 413
mucosa in, 477
myxomatous, 413
nutrition in, 417
"occult blood" in, 416
onset of, 415
pain in, 416
treatment of, 431
palpation in, 418
pathology of, 411
percussion in, 419
perforation in, 413
prognosis of, 429
pus in, 416
pyloric stenosis and, 467
race in, 409
sarcinæ in, 421
scirrhus, 412
secondary, 411
sex in, 410
Stomach, carcinoma of, simplex, 412
site of, 411
squamous-celled, 413
stomach contents in, 419
symptoms of, 414
thirst in, 415
tongue in, 415
trauma and, 410
treatment of, 429
lavage in, 430
mechanical, 430
medical, 429
palliative, 433
results of, 433
roentgen-ray, 431
surgical, 431
tumor in, 418
ulcer and, 394, 410
urine in, 417
vomiting in, 415
yeast cells in, 422
cardia of, carcinoma of, diagnosis of, 428
symptoms of, 428
treatment of, 429
cirrhosis of, 478
abdomen in, 482
age and, 479
ascites in, 482
chronic gastritis and, 450
circumscribed, 481
diagnosis of, 483
from syphilis, 484
jaundice in, 483
lymphatics in, 481
mucosa in, 480
muscularis in, 480
nomenclature of, 478
pain in, 482
pathogenesis of, 479
pathology of, 480
peristalsis in, 482
sex in, 479
submucosa in, 480
symptoms of, 482
syphilis and, 479
trauma and, 479
treatment of, 484
tumor in, 482
vomiting in, 482
dilatation of, 456
acute, 231, 457
breath in, 250
cardiospasm and, 460
constipation in, 460
debilitating conditions in, 459
deformities of spine and, 459
diagnosis of, 460
dietetic errors and, 460
distention in, 460
dyspnœa in, 460
etiology of, 457
inspection in, 460
kidney and, 460
lavage in, 461
operations and, 461

Stomach, dilatation of, acute, pain in, 460
palpation in, 460
pancreas and, 460
pathology of, 460
percussion in, 460
postnarcotic, 458
postoperative, 458
prognosis of, 461
pylorospasm and, 460
symptoms of, 460
traction on duodenum and, 458
trauma in, 459
treatment of, 461
vomiting in, 460
chronic, 461
constipation in, treatment of, 471
diagnosis of, 465
from chronic gastritis, 466
from dilated colon, 465
from dilatation of œsophagus, 466
from gastric crises, 466
from gastroptosis, 466
from hypersecretion, 466
from nervous dyspepsia, 466
etiology of, 462
foreign bodies and, 462
gastrectasis and, 462
gastroptosis and, 462
hypertrophic pyloric stenosis and, 462
idiopathic, 462
mucous membrane in, 463
nephroptosis and, 995
obstructive, 462
constipation in, 463
diarrhœa in, 463
pain, 464
symptoms of, 463
nervous, 464
tetany in, 464
prognosis of, 465
treatment of, 465
urine in, 464
vomiting in, 464
pathology of, 463
perigastritis and, 462
prognosis of, 468
prophylaxis in, 469
relative, 462
spasm and, 462
symptomatic, 462
symptoms of, 463
treatment of, 469
diet in, 469
drugs in, 471
electricity in, 477
hydrotherapy in, 470
mechanical, 470
surgical, 471
tumors of gall-bladder and, 462
of liver and, 462
Stomach, dilatation of, chronic, tumor of pancreas and, 462
varieties of, 461
vomiting in, treatment of, 471
definition of, 456
diagnosis of, from atony, 366
diseases of, acute peritonitis and, 911
constipation and, 521
diarrhœa and, 534
functional, 307
organic, 371
distention of, 355. *See* Pneumatosis.
hour-glass, 396
hyperacidity of, 314. *See* Hyperacidity.
hyperchlorhydria of, 314. *See* Hyperacidity.
hypersecretion of, 323
hypochlorhydria of, 556. *See* Hypochlohydria.
lesser curvature of, carcinoma of, diagnosis of, 428
motor insufficiency of, forms of, 456
mucous membrane of, dilatation and, 463
mucus hypersecretion in, 330
nerve supply of, 307
neuroses of, 307. *See* Gastric neurosis.
in obesity, 211
pylorus of, incontinence of, 364
spasm of, 351. *See* Pylorospasm.
stenosis of, 466. *See* Pylorus, stenosis of.
secretion of, 235
endocrine glands and, 316
foods exciting, 321
subacidity of, 356. *See* Hypochlorhydria.
sympathetic system and, 307
syphilis of, 491
age and, 492
anorexia in, 493
diagnosis of, 493
diffuse infiltration in, 491
emaciation in, 493
gastric analysis in, 493
gumma in, 491
hematemesis in, 493
lesions in, 491
pain in, 492
roentgen-ray examination in, 493
sequelæ of, 492
sex and, 492
site of, 492
symptoms of, 492
treatment of, 494
vomiting in, 493
ulcer of, 371. *See* also Gastric ulcer.
diagnosis of, from hyperacidity, 319
from nervous dyspepsia, 369
gastralgia, 336
varices in, hematemesis from, 488
Stomatitis, aphthous, 254
confluent, 255

Stomatitis, aphthous, etiology of, 254
symptoms of, 254
treatment of, 255
catarrhal, 253
pathology of, 254
symptoms of, 254
treatment of, 254
gangrenous, 256
bacteriology of, 257
symptoms of, 257
treatment of, 257
gonorrhœal, 259
treatment of, 259
herpetic, 259
hypomycetic, 258
mercurial, 256
treatment of, 256
mucofibrinous, 254
mycotic, 258
ulcerative, 255
bacteriology of, 255
symptoms of, 256
treatment of, 256
Stomatopharyngitis herpetica, 259
herpetiformis, 259
Strangulation of intestines, 600
hemorrhage from, 517
Streptococcal glossitis, chronic, 270
Streptococcus pyogenes in acute peritonitis, 913
in appendicitis, 569
Stricture of intestines, 600
obstruction from, 613
of œsophagus, cicatricial, 298
congenital, 285
Strongyloides stercoralis in sprue, 649
Subacidity, 356. *See* Hypochlohydria.
Subphrenic abscess, 937
boundaries of, 941
left anterior intraperitoneal, 941
extraperitoneal, 943
posterior intraperitoneal, 942
position of, 941
right anterior, 941
extrahepatic, 943
rupture of, 944
without gaseous contents, 938
abscess of liver and, 939
of pancreas and, 939
of spleen and, 939
age in, 940
appendicitis and, 938
bacteriology of, 945
diagnosis of, 946
from empyema, 947
from pleural effusion, 947
duodenal ulcer and, 939
empyema and, 940
etiology of, 938
fever in, 945
gastric ulcer and, 939
onset of, 946
pain in, 945
pathology of, 940
pericolic abscess and, 939
prognosis of, 948
Subphrenic abscess, without gaseous contents, pulmonary embolism in, 946
pulse in, 946
retroperitoneal abscess and, 940
sex in, 940
symptoms of, 945
treatment of, 948
tuberculosis of spine and, 940
pyopneumothorax, 948
abdomen in, 949
age and, 950
appendicular abscess and, 949
diagnosis of, 951
from diaphragmatic hernia, 952
from pleural effusion, 951
duodenal ulcer and, 949
etiology of, 948
fever in, 950
gastric ulcer and, 949
hydatid cyst of liver and, 949
leukocytosis in, 950
onset of, 950
pain in, 950
parotitis in, 951
pathology of, 949
pleuritis in, 951
prognosis of, 952
sex and, 950
symptoms of, 950
treatment of, 952
vomiting in, 950
Succus entericus, 499
Sugar in blood, 46, 132
in diabetes mellitus, 133
consumption, diabetes mellitus and, 119
in urine in diabetes mellitus, 142
Sugar-iced liver, 783
Sugars, metabolism of, intermediary, 45
Superalimentation, digestion and, 243
Supracapillary carcinoma of duodenum, 634
Suppurative cholangitis, 849
cholecystitis, 855
hepatitis, 790. *See* Liver, abscess of.
pancreatitis, 681
diagnosis of, from hemorrhagic necrosis, 679
phlebitis of hepatic veins, 755
pylephlebitis, 758
diagnosis of, from suppurative cholangitis, 851
tuberculosis of peritoneum, 963
Surface area, determination of, 75
Sweating in abscess of liver, 794
Sympathetic system, stomach and, 307
Sympathicotonia, 308
carbohydrate metabolism in, 127
Syphilis, acute yellow atrophy of liver and, 768
atrophy of tongue and, 274
chronic perihepatitis and, 783
peritonitis and, 958
cirrhosis of liver and, 802

Syphilis, cirrhosis of stomach and, 479
congenital, Hutchinsonian teeth in, 266
diabetes insipidus and, 171
mellitus and, 119, 120, 124
diagnosis of, from cirrhosis of stomach 784
of intestines, 598
leukoplakia and, 273
of liver, diagnosis of, from carcinoma, 837
from perihepatitis, 787
of mouth, 265
of œsophagus, 289
of pancreas, 692
of rectum, 598
of salivary glands, 278
of stomach, 491
Systemic circulation, biliary infections through, 843

T

Tabes dorsalis, diabetes mellitus and, 121
mouth in, 264
pseudo-, in diabetes mellitus, 148
Tænia echinococcus in cysts of peritoneum, 972
Taste, disturbances of, 251
Teeth, Hutchinson's, 266
Telangiectasis in jaundice, 739
Tenderness in acute peritonitis, 918
Tenesmus in diarrhœa, 536
in intussusception, 618
Thirst in acute peritonitis, 917
in carcinoma of stomach, 415
in diabetes insipidus, 175
mellitus, 140
Thrombophlebitis in diabetes mellitus, 147
of hepatic veins, 755
Thrombosis of hepatic artery, 753
veins, 755
of mesenteric arteries, 641
intestinal hemorrhage and, 517
of portal vein, 755
diagnosis of, from cirrhosis of liver, 819
Thrombotic ulcers of intestines, 559
Thrush, 258
diagnosis of, 258
symptoms of, 258
treatment of, 258
Thyroid gland, carbohydrate metabolism and, 129
diabetes mellitus and, 129
diseases of, basal metabolism and, 102
hyposecretion, obesity and, 210
obesity, 215
tumors of tongue, 274
Thyroxin, metabolism and, 102
Tinea circinata of mouth, 262
Tissot spirometer, 27
Tissue necrosis in gout, 191
Tongue, anomalies of, 268
atrophy of, 274
black, 269
carcinoma of, 274
cavernous angioma of, 268
doubling of, 268
fibroma of, 274
frenum of, deformities of, 268
ulcer of, 271
geographical, 271
hemorrhage from, 269
hyperkeratosis of, 269
melanotrichia of, 269
pain in, 272
paralysis of, 269
Riga's disease of, 274
sarcoma of, 274
scrotal, 269
spasm of, 269
in sprue, 652
sucking, 269
swallowing, 269
tuberculosis of, 265
tumors of, 274
varicose veins of, 269
wandering rash of, 271
Tonic contractions of intestines, 497
Tophi in gout, 192, 199
Torus palatinus, 259
Toxemia in cirrhosis of liver, 814
obstruction of intestines and, 601
Toxic gastritis, 441
jaundice, 732
Traction on duodenum, dilatation of stomach and, 458
Transudates in ascites, 898
Trauma, abscess of liver and, 792
acute dilatation of stomach and, 459
carcinoma of stomach and, 410
cirrhosis of stomach and, 479
diabetes mellitus and, 121
in gastric ulcer, 374
gout and, 180
of œsophagus, 288
Traumatic cysts of pancreas, 702
œsophagitis, 285
Trench mouth, 263
Treponema pallidium in mouth, 266
Trichuris trichiura, appendicitis and, 568
Trophic ulcers of intestines, 561
Tropical abscess of liver, 793
Trypsin, 498
Tuberculosis of appendix, 592
breath in, 250
chronic peritonitis and, 956
cirrhosis of liver and, 810, 817
in diabetes mellitus ,138, 148
treatment of, 168
fatty liver and, 762, 763
of gums, 264
of intestines, 594
of lips, 264
of mouth, 264
of œsophagus, 288
of pancreas, 692
of peritoneum, 959
diagnosis of, from cirrhosis of liver, 819

Tuberculosis of peritoneum, diagnosis of, from perihepatitis, 787
of salivary glands, 278
of soft palate, 265
of spine, subphrenic abscess and, 940
of tongue, 265
Tuberculous meningitis, diabetes insipidus and, 172
pleuritis in cirrhosis of liver, 817
Tubular diarrhœa, 644
Tumors in appendicitis, 578
of appendix, 593
in carcinoma of intestines, 636
of pancreas, 710, 711
in cirrhosis of stomach, 482
in cysts of pancreas, 703
of gall-bladder, diagnosis of, from carcinoma of stomach, 427
dilatation of stomach and, 462
in gangrenous pancreatitis, 678
in hypertrophic stenosis of pylorus, 475
of intestine, benign, 639
malignant, 631
of lips, 253
of liver, benign, 838
dilatation of stomach and, 462
malignant, 833
mixed, of salivary glands, 278
of mouth, 260
in necrosis of pancreas, 676
of œsophagus, benign, 303
of omentum, diagnosis of, from carcinoma of stomach, 427
of pancreas, dilatation of stomach and, 462
of parotid gland, mixed, 279
of peritoneum, 968
diagnosis of, from carcinoma of stomach, 427
from cirrhosis of liver, 819
from tuberculosis, 966
malignant, 979
primary, 979
secondary, 982
non-malignant, 969
solid, 969
phantom, 510
of salivary glands, 279
in suppurative pancreatitis, 684
of tongue, 274
of liver, dilatation of stomach and, 462
Tylosis linguæ, 272
Tympanites, 509
in acute peritonitis, 919
diagnosis of, from acute peritonitis, 926
Typhoid bacillus, acute cholecystitis and, 854
fever, biliary tract in, 854
cirrhosis of liver and, 802
diagnosis of, from appendicitis, 586
from tuberculosis of peritoneum, 965
metabolism in, 101
mouth in, 262

U

Ulcer, duodenal, 404, 554
diagnosis of, from aneurism of hepatic artery, 754
from cholelithiasis, 880
from cirrhosis of liver, 818
from hyperacidity, 319, 320
from obstruction of intestines, 558
subphrenic abscess and, 939
pyopneumothorax and, 949
of frenum of tongue, 271
gastric, 232, 371
chronic peritonitis and, 952
diagnosis of, from cholelithiasis, 892
from cirrhosis of liver, 819
intestinal hemorrhage and, 518
subphrenic abscess and, 939
pyopneumothorax and, 949
of intestine, 553
catarrhal, 560
embolic, 559
follicular, 560
gastro-jejunal, 559
thrombotic, 559
trophic, 561
tuberculous, 595
uremic, 559
of œsophagus, 287
diagnosis of, from hematemesis, 487
peptic, 371
of pylorus, diagnosis of, from carcinoma of stomach, 428
round, 371
of stomach, diagnosis of, from nervous dyspepsia, 369
gastralgia, 336
perforating, 371
Ulcerative cholecystitis, 856
stomatitis, 255
tuberculosis of peritoneum, 963
Uncinaria duodenalis, cirrhosis of liver and, 802
Undernutrition, protein metabolism in, 61
Urachal cysts of peritoneum, 978
Urate crystals in gout, 199
deposits in gout, 191, 194
Urea in protein metabolism, 62
Urea-forming function of liver, 721
Uremia, breath in, 250
diagnosis of, from acute peritonitis, 927
in gout, 198
mouth in, 262
Uremic ulcers of intestines, 559
Uric acid, 63
in blood, 185
in gout, 186
in diabetes mellitus, 144
endogenous, 63
excretion of, 181
in gout, 187
metabolism in gout, 182, 186

Uric acid metabolism, normal, 181
purins and, 184, 185, 188
in urine in gout, excretion of, 187
Urine in abscess of liver, 795
in acute catarrhal cholangitis, 845
hepatitis, 789
peritonitis, 922
yellow atrophy of liver, 771
in appendicitis, 579
in carcinoma of stomach, 417
in chronic perihepatitis, 786
in cirrhosis of liver, 817, 829
in congestion of liver, 778
in diabetes mellitus, 142
acetone in, 144
albumin in, 145
alloxuric bodies in, 145
ammonia in, 144
β-oxybutyric acid in, 144
casts in, 145
diacetic acid in, 144
glycogen in, 146
glycuronic acid in, 144
lipuria in, 146
nitrogen in, 144
pneumaturia in, 146
sodium chloride in, 145
phosphate in, 145
sulphate in, 145
sugar in, 142
uric acid in, 144
in diagnosis of intestinal obstruction, 609
in dilatation of stomach, 464
fat-splitting ferment in, 668
in gastric ulcer, 382
glucose in, tests for, 143
in gout, 197
in hyperacidity, 319
in jaundice, 740
in necrosis of pancreas, 676
in nephroptosis, 995
in toxic gastritis, 442
in tuberculosis of peritoneum, 964
Urobilinuria in jaundice, 740
Urticaria in jaundice, 739
of mouth, 260
Uterus, perforation of, acute peritonitis and, 911
rupture of periappendicular abscess into, 572

V

Vagotonia, 308
carbohydrate metabolism in, 127
in pylorospasm, 351
van den Bergh's liver functional tests, 726
Varicella, mouth in, 264
Varices of œsophagus, 289
diagnosis of, from hematemesis, 487
Varicose veins of tongue, 269
Variola, mouth in, 264
Vascular spasm, gastric ulcer and, 375
Vater, ampulla of, carcinoma of, 888
Vater, diverticulum of, biliary tract infection through, 842
Veins in obesity, 211
Venous mesenteric thrombosis, 641
stasis, hematemesis from, 488
Vicarious hemorrhages, diagnosis of, from hematemesis, 488
Visceroptosis, 986. *See* Splanchnoptosis.
congenital origin of, 987
digestion and, 242
neurasthenia and, 992
respiration and, 988
Vitamines, basal metabolism and, 86
metabolism and, 29
pellagra and, 91
rickets and, 90
scurvy and, 90
Volvulus, 618
constipation in, 620
diagnosis of, 620
diarrhœa in, 620
etiology of, 619
of omentum, 624
pain in, 620
pathology of, 619
prognosis of, 620
seats of, 619
symptoms of, 620
vomiting in, 620
Vomiting in active congestion of liver, 774
in achylia gastrica, 359
in acute cholecystitis, 857
dilatation of stomach, 460
enteritis, 540
gastritis, 436
hepatitis, 789
perihepatitis, 781
peritonitis, 920
yellow atrophy of liver, 771
in appendicitis, 576
in carcinoma of liver, 835
of pancreas, 711
of stomach, 415
in catarrhal cholangitis, 846
central, 343
centre, 342
cerebrospinal, 343
in cholera nostras, 541
in chronic gastritis, 450
in cirrhosis of liver, 812, 828
of stomach, 482
in congenital hypertrophic stenosis of pylorus, 475
in constipation, 525
in diarrhœa in childhood, 550
in dilatation of stomach, 464
in duodenal ulcer, 406, 556
in fatty liver, 763
fecal, 605
in gall-stone colic, 871
in gastric ulcer, 382
in gastrosuccorrhœa, 324
in hemoperitoneum, 908
in hyperacidity, 319
in interstitial pancreatitis, 690
in intestinal colic, 515
indigestion, 512

Vomiting, juvenile, 345
in mesenteric embolism, 642
thrombosis, 642
in mycotic gastritis, 443
in necrosis of pancreas, 676
in nephroptosis, 995
nervous, 342, 344
diagnosis of, 345
etiology of, 343
prognosis of, 345
treatment of, 346
in obstruction of intestines, 605
periodical, 344
in children, 345
in phlegmonous gastritis, 440
psychic, 344
in pylorospasm, 352
reflex, 345
in splanchnoptosis, 992
in subphrenic pyopneumothorax, 950
in suppurative pancreatitis, 683
pylephlebitis, 759
in syphilis of stomach, 493
in thrombosis of portal vein, 757
in toxic gastritis, 442
in volvulus, 620

W

Wandering rash of tongue, 231
Water drinking at meals, metabolism and, 68
Water intake, metabolism and, 66
output, metabolism and, 66
starvation, 31
Waxes, 48
Webs of œsophagus, congenital, 285
White bile, 741
Widal's liver functional test, 731
Wilson's disease, 831
hepatic cirrhosis in, 832

X

Xanthin bases, 181
Xanthoma in diabetes mellitus, 147
Xerophthalmia, 90
Xerostomia, 276
etiology of, 277
treatment of, 277

Y

Yeast cells in carcinoma of stomach, 422
Yellow atrophy of liver, acute, 767

Z

Zuntz-Geppert respiration apparatus, 27